Access GS# 97285

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name Rebecca Lorke Examiner #: _____ Date: 6/23/03

Art Unit: 1614 Phone Number 305 4729 Serial Number: 10/089436

Mail Box and Bldg./Room Location 6M 1 2D01 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. ME'

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): Tstvan S. Szelenyi

Earliest Priority Filing Date: 9/30/99

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please provide structure for compounds of claims 1 & 3 & search each separately & together to treat disorders of claims 5 & 11

Thanks
Rebecca

RECEIVED
JUN 24 2003
(STIC)

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher:	NA Sequence (#)	STN
Searcher Phone #:	AA Sequence (#)	Dialog
Searcher Location:	Structure (#)	Questel/Orbit
Date Searcher Picked Up:	Bibliographic	Dr. Links
Date Completed:	Litigation	Lexis/Nexis
Searcher Prep & Review Time:	Fulltext	Sequence Systems
Clerical Prep Time:	Patent Family	WWW/Internet
Online Time:	Other	Other (specify)

=> fil reg; d ide 1-2
FILE 'REGISTRY' ENTERED AT 12:21:59 ON 26 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 JUN 2003 HIGHEST RN 537653-06-8
DICTIONARY FILE UPDATES: 25 JUN 2003 HIGHEST RN 537653-06-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

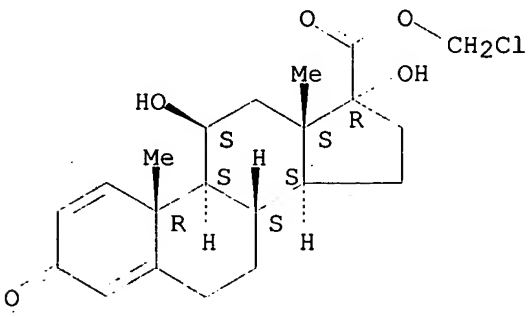
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

L1 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 129260-79-3 REGISTRY
CN Androsta-1,4-diene-17-carboxylic acid, 11,17-dihydroxy-3-oxo-, chloromethyl ester, (11.beta.,17.alpha.)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Loteprednol**
FS STEREOSEARCH
MF C21 H27 Cl O5
SR World Health Organization
LC STN Files: ADISINSIGHT, ADISNEWS, BIOBUSINESS, BIOSIS, CA, CAPLUS, CIN, DIOGENES, DRUGPAT, DRUGUPDATES, PROMT, SYNTHLINE, TOXCENTER, USAN, USPATFULL

Absolute stereochemistry.



514/179

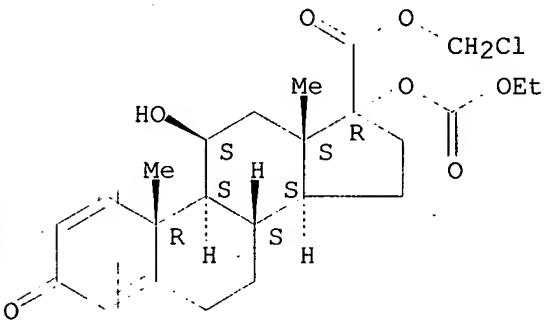
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

12 REFERENCES IN FILE CA (1957 TO DATE)
13 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 82034-46-6 REGISTRY
CN Androsta-1,4-diene-17-carboxylic acid, 17-[(ethoxycarbonyl)oxy]-11-hydroxy-

3-oxo-, chloromethyl ester, (11.beta.,17.alpha.)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN CDDD 5604
CN HGP 1
CN Lenoxin
CN **Loteprednol etabonate**
CN P 5604
FS STEREOSEARCH
MF C24 H31 Cl O7
LC STN Files: ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.

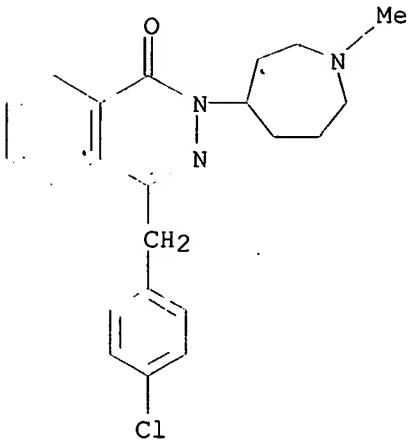


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

53 REFERENCES IN FILE CA (1957 TO DATE)
53 REFERENCES IN FILE CAPLUS (1957 TO DATE)

=> d ide

L2 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 79307-93-0 REGISTRY
CN 1(2H)-Phthalazinone, 4-[(4-chlorophenyl)methyl]-2-(hexahydro-1-methyl-1H-azepin-4-yl)-, monohydrochloride (9CI) (CA INDEX NAME)
OTHER NAMES:
CN A 5610
CN Allergodil
CN Astelin
CN **Azelastine hydrochloride**
CN Azeptin
CN E 0659
CN Rhinolast
CN W 2979M
MF C22 H24 Cl N3 O . Cl H
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CIN, DIOGENES, DRUGPAT, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PHARMASEARCH, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
CRN (58581-89-8)



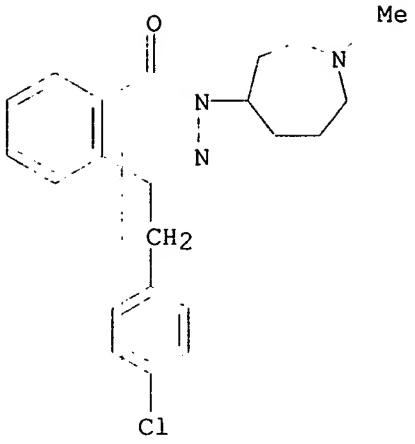
514/217.05

● HCl

84 REFERENCES IN FILE CA (1957 TO DATE)
86 REFERENCES IN FILE CAPLUS (1957 TO DATE)

=> d ide 2

L2 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 58581-89-8 REGISTRY
CN 1(2H)-Phthalazinone, 4-[(4-chlorophenyl)methyl]-2-(hexahydro-1-methyl-1H-azepin-4-yl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (.+-.)-Azelastine
CN **Azelastine**
FS 3D CONCORD
DR 153483-42-2
MF C22 H24 Cl N3 O
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



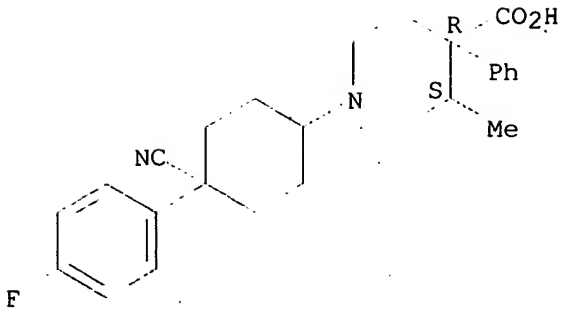
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

354 REFERENCES IN FILE CA (1957 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
359 REFERENCES IN FILE CAPLUS (1957 TO DATE)

=> d ide 1-2

L3 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 79547-78-7 REGISTRY
CN 4-Piperidinecarboxylic acid, 1-[cis-4-cyano-4-(4-fluorophenyl)cyclohexyl]-3-methyl-4-phenyl-, monohydrochloride, (3S,4R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 4-Piperidinecarboxylic acid, 1-[4-cyano-4-(4-fluorophenyl)cyclohexyl]-3-methyl-4-phenyl-, monohydrochloride, [3S-[1(cis),3.alpha.,4.beta.]]-
OTHER NAMES:
CN **Levocabastine hydrochloride**
CN Livostin
FS STEREOSEARCH
MF C26 H29 F N2 O2 . Cl H
LC STN Files: ADISINSIGHT, BEILSTEIN*, BIOSIS, CA, CAPLUS, CIN, DIOGENES, DRUGPAT, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PHARMASEARCH, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
CRN (79516-68-0)

Absolute stereochemistry.



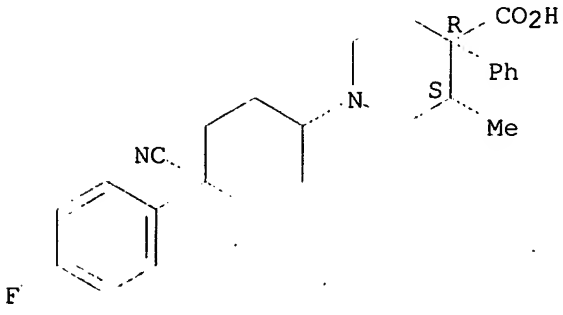
514/330

● HCl

18 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
18 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 79516-68-0 REGISTRY
CN 4-Piperidinecarboxylic acid, 1-[cis-4-cyano-4-(4-fluorophenyl)cyclohexyl]-3-methyl-4-phenyl-, (3S,4R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 4-Piperidinecarboxylic acid, 1-[4-cyano-4-(4-fluorophenyl)cyclohexyl]-3-methyl-4-phenyl-, [3S-[1(cis),3.alpha.,4.beta.]]-
OTHER NAMES:
CN **Levocabastine**
CN Levophta
CN R 50547
FS STEREOSEARCH
MF C26 H29 F N2 O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

132 REFERENCES IN FILE CA (1957 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
134 REFERENCES IN FILE CAPLUS (1957 TO DATE)

```
=> fil drugu biotechno caba ipa biosis toxcenter
FILE 'DRUGU' ENTERED AT 12:57:53 ON 26 JUN 2003
COPYRIGHT (C) 2003 THOMSON DERWENT

FILE 'BIOTECHNO' ENTERED AT 12:57:53 ON 26 JUN 2003
COPYRIGHT (C) 2003 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'CABA' ENTERED AT 12:57:53 ON 26 JUN 2003
COPYRIGHT (C) 2003 CAB INTERNATIONAL (CABI)

FILE 'IPA' ENTERED AT 12:57:53 ON 26 JUN 2003
COPYRIGHT (C) 2003 American Society of Hospital Pharmacists (ASHP)

FILE 'BIOSIS' ENTERED AT 12:57:53 ON 26 JUN 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'TOXCENTER' ENTERED AT 12:57:53 ON 26 JUN 2003
COPYRIGHT (C) 2003 ACS

=> d que l85
L1             2 SEA FILE=REGISTRY ABB=ON  LOTEPREDNOL?/CN
L2             2 SEA FILE=REGISTRY ABB=ON  AZELASTINE/CN OR "AZELASTINE
                 HYDROCHLORIDE"/CN
L3             2 SEA FILE=REGISTRY ABB=ON  LEVOCABASTINE?/CN
L80          218 SEA LOTEPREDNOL# OR LOTEMAX OR ALREX OR LENOXIN OR CDDD5604 OR
                 CDDD 5604 OR HGP1 OR HGP 1 OR P5604 OR P 5604 OR L1
L81         1743 SEA AZELASTIN# OR A 5610 OR A5610 OR ASTELIN# OR OPTIVAR# OR
                 ALLERGODIL# OR ASTELIN#
L82         1259 SEA AZEPTIN# OR "E0659" OR E 0659 OR W2979M OR W 2979M OR
                 RHINOLAST# OR L2
L83          737 SEA LEVOCABASTIN# OR LIVOSTIN# OR LEVOPHTA OR R50547 OR R
                 50547 OR L3
L85            2 SEA L80 AND (L81 OR L82 OR L83)


=> fil medl
FILE 'MEDLINE' ENTERED AT 12:58:00 ON 26 JUN 2003

 FILE LAST UPDATED: 25 JUN 2003 (20030625/UP).  FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que 168; fil embase; d que 145; fil capl; d que 153; dup rem 153,185,145
L1             2 SEA FILE=REGISTRY ABB=ON  LOTEPREDNOL?/CN
L2             2 SEA FILE=REGISTRY ABB=ON  AZELASTINE/CN OR "AZELASTINE
                 HYDROCHLORIDE"/CN
L3             2 SEA FILE=REGISTRY ABB=ON  LEVOCABASTINE?/CN
L4            52 SEA FILE=MEDLINE ABB=ON  LOTEPREDNOL# OR LOTEMAX OR ALREX OR
                 LENOXIN OR CDDD5604 OR CDDD 5604 OR HGP1 OR HGP 1 OR P5604 OR
                 P 5604 OR L1
L5           444 SEA FILE=MEDLINE ABB=ON  AZELASTIN# OR A 5610 OR A5610 OR
                 ASTELIN# OR OPTIVAR# OR ALLERGODIL# OR ASTELIN#
L6           352 SEA FILE=MEDLINE ABB=ON  AZEPTIN# OR "E0659" OR E 0659 OR
                 W2979M OR W 2979M OR RHINOLAST# OR L2
L7           212 SEA FILE=MEDLINE ABB=ON  LEVOCABASTIN# OR LIVOSTIN# OR
```

```
                LEVOPHTA OR R50547 OR R 50547 OR L3
L68           0 SEA FILE=MEDLINE ABB=ON  L4 AND (L5 OR L6 OR L7)


FILE 'EMBASE' ENTERED AT 12:58:29 ON 26 JUN 2003
COPYRIGHT (C) 2003 Elsevier Science B.V.  All rights reserved.

 FILE COVERS 1974 TO 19 Jun 2003 (20030619/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L31         118 SEA FILE=EMBASE ABB=ON  LOTEPREDNOL ETABONATE/CT
L32        1007 SEA FILE=EMBASE ABB=ON  AZELASTINE/CT
L33         568 SEA FILE=EMBASE ABB=ON  LEVOCABASTINE/CT
L35        1178 SEA FILE=EMBASE ABB=ON  ALLERGIC CONJUNCTIVITIS/CT
L36        1720 SEA FILE=EMBASE ABB=ON  ANTIALLERGIC AGENT/CT
L37      518140 SEA FILE=EMBASE ABB=ON  RESPIRATORY TRACT DISEASE+NT/CT
L38         607 SEA FILE=EMBASE ABB=ON  RHINOCONJUNCTIVITIS/CT
L39        7418 SEA FILE=EMBASE ABB=ON  ALLERGIC RHINITIS/CT
L40       23641 SEA FILE=EMBASE ABB=ON  ALLERGY/CT
L45          15 SEA FILE=EMBASE ABB=ON  L31 AND (L35 OR L36 OR L37 OR L38 OR
                L39 OR L40) AND (L32 OR L33)


FILE 'CAPLUS' ENTERED AT 12:58:29 ON 26 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 26 Jun 2003  VOL 138 ISS 26
FILE LAST UPDATED: 25 Jun 2003  (20030625/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


L1            2 SEA FILE=REGISTRY ABB=ON  LOTEPREDNOL?/CN
L2            2 SEA FILE=REGISTRY ABB=ON  AZELASTINE/CN OR "AZELASTINE
                HYDROCHLORIDE"/CN
L3            2 SEA FILE=REGISTRY ABB=ON  LEVOCABASTINE?/CN
L49          63 SEA FILE=CAPLUS ABB=ON  L1
L50         423 SEA FILE=CAPLUS ABB=ON  L2
L51         146 SEA FILE=CAPLUS ABB=ON  L3
L53           3 SEA FILE=CAPLUS ABB=ON  L49 AND (L50 OR L51)
```

FILE 'CAPLUS' ENTERED AT 12:58:29 ON 26 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'DRUGU' ENTERED AT 12:58:29 ON 26 JUN 2003
COPYRIGHT (C) 2003 THOMSON DERWENT

FILE 'TOXCENTER' ENTERED AT 12:58:29 ON 26 JUN 2003
COPYRIGHT (C) 2003 ACS

FILE 'EMBASE' ENTERED AT 12:58:29 ON 26 JUN 2003
COPYRIGHT (C) 2003 Elsevier Science B.V. All rights reserved.
PROCESSING COMPLETED FOR L53
PROCESSING COMPLETED FOR L85
PROCESSING COMPLETED FOR L45
L86 19 DUP REM L53 L85 L45 (1 DUPLICATE REMOVED)
ANSWERS '1-3' FROM FILE CAPLUS
ANSWER '4' FROM FILE DRUGU
ANSWERS '5-19' FROM FILE EMBASE

=> d ibib ab hitrn 1-3; d iall 4-19

L86 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 2002:555949 CAPLUS
DOCUMENT NUMBER: 137:113508
TITLE: Methods and apparatus for applying medication of nasal sinuses
INVENTOR(S): Dyer, Gordon Wayne
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 4 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002098154	A1	20020725	US 2001-765894	20010120

PRIORITY APPLN. INFO.: US 2001-765894 20010120

AB The present invention provides a method and accompanying app. for supplying medications, particularly antibiotics, to the deeper parts areas of the sinuses. The pressure of application from use of the Valsalva maneuver and the use of medications that are both H2O and fat-sol. aids the medications in penetrating deep into the sinuses. When the medication is an antibiotic, this has the benefit of delivering a high level of antibiosis using a line of antibiotics that the likely bacteria will not be as resistant to because they have not had as much prior exposure to this antibiotic. The lighter-than-air propellant aids in delivering the medication to those sinus areas superior to the nose. If the infection extends to the eardrums, making the Valsalva maneuver painful, or if the patient is simply unusually sensitive, then earplugs to reduce the stress on the eardrums may be worn while the patient performs the Valsalva maneuver.

IT **79516-68-0**, Levocabastine
RL: EPR (Engineering process); NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); TEM (Technical or engineered material use); PROC (Process); USES (Uses)
(ketotifen; methods and app. for applying medication of nasal sinuses)
IT **82034-46-6**, Loteprednol etabonate

RL: EPR (Engineering process); NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); TEM (Technical or engineered material use); PROC (Process); USES (Uses)
(methods and app. for applying medication of nasal sinuses)

L86 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:472413 CAPLUS
TITLE: Compositions containing a histamine H1 antagonist and a steroid for rhinitis treatment
INVENTOR(S): Yanni, John M.; Gamache, Daniel A.; Miller, Steven T.
PATENT ASSIGNEE(S): Alcon, Inc., Switz.
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003049770	A1	20030619	WO 2002-US36915	20021118

W: AU, BR, CA, CN, JP, KR, MX, PL, US, ZA
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR

PRIORITY APPLN. INFO.: US 2001-337371P P 20011205
AB Compns. and methods for treating rhinitis with H1 antagonists/antiallergics and steroids are disclosed. Thus, a formulation contained emedastine 0.05, rimexolone 0.1, benzalkonium chloride 0.01, tromethamine 0.5, disodium EDTA 0.01, NaCl 0.6-0.8, HPMC 0.1-0.5, Tyloxapol 0.05, NaOH and/or HCl qs to pH 7.4, and water to 100%.
IT INDEXING IN PROGRESS
IT **58581-89-8**, Azelastine **79516-68-0**, Levocabastine **129260-79-3**, Loteprednol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. histamine H1 antagonist and steroid for rhinitis treatment)

L86 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:247171 CAPLUS
DOCUMENT NUMBER: 134:256898
TITLE: Combination of loteprednol and antihistamines for the local treatment of allergies and respiratory tract diseases
INVENTOR(S): Szelenyi, Istvan; Marx, Degenhard; Heer, Sabine; Engel, Juergen
PATENT ASSIGNEE(S): Asta Medica Ag, Germany
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001022955	A2	20010405	WO 2000-EP9391	20000926
WO 2001022955	A3	20010517		

W: AU, BG, BR, BY, CA, CN, CZ, DZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

DE 19947234	A1	20010405	DE 1999-19947234	19990930

Searched by Barb O'Bryen, STIC 308-4291

BR 2000014312	A	20020521	BR 2000-14312	20000926
EP 1216046	A2	20020626	EP 2000-969303	20000926
EP 1216046	B1	20030604		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY

JP 2003510275	T2	20030318	JP 2001-526167	20000926
EE 200200146	A	20030415	EE 2002-146	20000926

PRIORITY APPLN. INFO.: DE 1999-19947234 A 19990930
WO 2000-EP9391 W 20000926

AB The invention relates to a novel combination of a soft steroid, esp. loteprednol, and at least one antihistamine such as e.g., azelastine and/or levocabastine, for simultaneous, sequential or sep. application for the local treatment of allergies and respiratory tract diseases, e.g., allergic rhinitis (rhinoconjunctivitis). Thus a nasal spray contained in g: azelastine hydrochloride 0.1000; loteprednoletabonate 1.000; Avicel RC 591 1.100; polysorbate 80 0.1000; sorbitol soln. 70% 6.000; sodiumedetate 0.0500; benzalkonium chloride 0.0200; water ot 100 mL.

IT **58581-89-8**, Azelastine **79307-93-0**, Azelastine hydrochloride **79516-68-0**, Levocabastine **82034-46-6**, Loteprednoletabonate **129260-79-3**, Loteprednol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(combination of loteprednol and antihistamines for local treatment of allergies and respiratory tract diseases)

L86 ANSWER 4 OF 19 DRUGU COPYRIGHT 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-35025 DRUGU T S E
TITLE: Ocular allergy guidelines. A practical treatment algorithm.
AUTHOR: Bielory L
CORPORATE SOURCE: Univ.New-Jersey-Med.+Dent.
LOCATION: Newark, N.J., USA
SOURCE: Drugs (62, No. 11, 1611-34, 2002) 3 Fig. 5 Tab. 219 Ref.
CODEN: DRUGAY ISSN: 0012-6667
AVAIL. OF DOC.: UMDNJ, Asthma and Allergy Research Center, Immuno-Opthalmology Service, New Jersey Medical School, Newark, New Jersey, U.S.A. (e-mail: bielory@umdnj.edu).
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

The treatment of ocular allergy is reviewed. Topics discussed are topical decongestants (phenylephrine, tetrahydrozoline, naphazoline and antazoline) antihistamines, dual (multiple)-acting agents, mast cell stabilizing agents, NSAIDS, tertiary treatment, routes of administration, ocular drug formulations and future developments. Drugs covered are loratadine, **levocabastine**, emedastine, olopatadine, ketotifen, **azelastine**, nedocromil, Na cromoglycate, lodoxamide, pemirolast, ketorolac, diclofenac, flurbiprofen, prednisolone, **loteprednol**-etabonate and acetyl-aspartyl-glutamate-N. Side-effects are also discussed. In conclusion, the future holds promise for additional advances with steroid-sparing immunomodulatory agents, especially in the more severe and chronic forms of ocular allergy. (No EX).

SECTION HEADING: T Therapeutics
S Adverse Effects
E Endocrinology

CLASSIF. CODE: 3 Antiallergics
35 Adverse Reactions

46 Corticosteroids
58 Vasoactive
62 Ophthalmological
64 Clinical Trials
69 Reviews

CONTROLLED TERM:

ALLERGY *TR; EYE-DISEASE *TR; CASES *FT; IN-VIVO *FT; REVIEW *FT; ANTIANAPHYLACTIC *FT; ANTIINFLAMMATORY *FT; VASOCONSTRICTOR *FT; CLIN.TRIAL *FT; CORTICOSTEROID *FT
[01] ANTIANAPHYLACTICS *FT; ANTIINFLAMMATORIES *FT; VASOCONSTRICTORS *FT; MAIN-TOPIC *FT; CORTICOSTEROIDS *FT; TR *FT; AE *FT
[02] LORATADINE *TR; **LEVOCABASTINE** *TR; EMEDASTINE *TR; OLOPATADINE *TR; KETOTIFEN *TR; **AZELASTINE** *TR; NEDOCROMIL *TR; CROMOLYN *TR; LODOXAMIDE *TR; PEMIROLAST *TR; KETOROLAC *TR; DICLOFENAC *TR; FLURBIPROFEN *TR; PREDNISOLONE *TR; **LOTEPREDNOL**-ETABONATE *TR; ACETYL-ASPARTYLGLUTAMATE-N *TR; LORATADINE *AE; **LEVOCABASTINE** *AE; EMEDASTINE *AE; OLOPATADINE *AE; KETOTIFEN *AE; **AZELASTINE** *AE; NEDOCROMIL *AE; CROMOLYN *AE; LODOXAMIDE *AE; PEMIROLAST *AE; KETOROLAC *AE; DICLOFENAC *AE; FLURBIPROFEN *AE; PREDNISOLONE *AE; **LOTEPREDNOL**-ETABONATE *AE; ACETYL-ASPARTYLGLUTAMATE-N *AE; TR *FT

FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L86 ANSWER 5 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003056371 EMBASE
TITLE: Conjunctival provocation testing: Overview of recent clinical trials in ocular allergy.
AUTHOR: Friedlaender M.H.
CORPORATE SOURCE: Dr. M.H. Friedlaender, Division of Ophthaymol, Scripps Clinic, 1066 North Torrey Pines Road, San Diego, CA 92037, United States
SOURCE: International Ophthalmology Clinics, (2003) 43/1 (95-104). Refs: 75
ISSN: 0020-8167 CODEN: IOPCAV
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 012 Ophthalmology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
*provocation test
*allergic disease: DI, diagnosis
*eye disease: DI, diagnosis
ocular pruritus: DT, drug therapy
allergic conjunctivitis: DT, drug therapy
vernal conjunctivitis: DT, drug therapy
drug mechanism
antiinflammatory activity
review
priority journal
Drug Descriptors:
*antihistaminic agent: DT, drug therapy
*antihistaminic agent: PD, pharmacology
*antihistaminic agent: PO, oral drug administration
*antihistaminic agent: TP, topical drug administration
*cromoglycate disodium: CM, drug comparison

*cromoglycate disodium: DT, drug therapy
*cromoglycate disodium: PD, pharmacology
*corticosteroid: DT, drug therapy
*corticosteroid: PD, pharmacology
*corticosteroid: TP, topical drug administration
*nonsteroid antiinflammatory agent: DT, drug therapy
*nonsteroid antiinflammatory agent: PD, pharmacology
naphazoline: DT, drug therapy
naphazoline: PD, pharmacology
histamine H1 receptor antagonist: DT, drug therapy
histamine H1 receptor antagonist: PD, pharmacology
antazoline: DT, drug therapy
antazoline: PD, pharmacology
pheniramine: DT, drug therapy
pheniramine: PD, pharmacology
levocabastine: CM, drug comparison
levocabastine: DT, drug therapy
levocabastine: PD, pharmacology
levocabastine: TP, topical drug administration
emedastine: DT, drug therapy
emedastine: PD, pharmacology
emedastine: TP, topical drug administration
loratadine: DT, drug therapy
loratadine: PD, pharmacology
loratadine: PO, oral drug administration
cetirizine: DT, drug therapy
cetirizine: PD, pharmacology
cetirizine: PO, oral drug administration
terfenadine: CM, drug comparison
terfenadine: DT, drug therapy
terfenadine: PD, pharmacology
terfenadine: PO, oral drug administration
ketorolac trometamol: DT, drug therapy
ketorolac trometamol: PD, pharmacology
lodoxamide: DT, drug therapy
lodoxamide: PD, pharmacology
olopatadine: DT, drug therapy
olopatadine: PD, pharmacology
nedocromil: DT, drug therapy
nedocromil: PD, pharmacology
nedocromil: TP, topical drug administration
azelastine: DT, drug therapy
azelastine: PD, pharmacology
fluorometholone: DT, drug therapy
fluorometholone: PD, pharmacology
fluorometholone: TP, topical drug administration
loteprednol etabonate: DT, drug therapy
loteprednol etabonate: PD, pharmacology
loteprednol etabonate: TP, topical drug administration
rimexolone: DT, drug therapy
rimexolone: PD, pharmacology
rimexolone: TP, topical drug administration
oxymetazoline: DT, drug therapy
oxymetazoline: PD, pharmacology
astemizole: DT, drug therapy
astemizole: PD, pharmacology
astemizole: PO, oral drug administration
tetryzoline: DT, drug therapy
tetryzoline: PD, pharmacology
tetryzoline: TP, topical drug administration
vasocon a
opcon a

visine a
levostin
lodoxamide trometamol
nedocromil sodium
ketotifen fumarate
pemirolast

CAS REGISTRY NO.: (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (naphazoline) 5144-52-5, 550-99-2, 835-31-4; (antazoline) 154-68-7, 2508-72-7, 3131-32-6, 91-75-8; (pheniramine) 86-21-5; (levocabastine) 79516-68-0; (emedastine) 87233-61-2, 87233-62-3; (loratadine) 79794-75-5; (cetirizine) 83881-51-0, 83881-52-1; (terfenadine) 50679-08-8; (ketorolac trometamol) 74103-07-4; (lodoxamide) 53882-12-5; (olopatadine) 113806-05-6, 140462-76-6; (nedocromil) 69049-73-6; (azelastine) 58581-89-8, 79307-93-0; (fluorometholone) 426-13-1; (loteprednol etabonate) 82034-46-6; (rimexolone) 49697-38-3; (oxymetazoline) 1491-59-4, 2315-02-8; (astemizole) 68844-77-9; (tetryzoline) 522-48-5, 84-22-0; (vasocon a) 60747-34-4; (lodoxamide trometamol) 63610-09-3; (nedocromil sodium) 69049-74-7; (ketotifen fumarate) 34580-14-8; (pemirolast) 69372-19-6

CHEMICAL NAME: Alrex; Acular; Optivar; Alamast; Zaditor; Alocril; Alomide; Patanol; Crolom; Emadine; Levostin; Visine a; Naphcon a; Opcon a; Vasocon a

L86 ANSWER 6 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003086939 EMBASE
TITLE: Topical nonsteroidal anti-inflammatory therapy in ophthalmology.
AUTHOR: Schalnus R.
CORPORATE SOURCE: Dr. R. Schalnus, Haager Weg 8, D-53127 Bonn, Germany. schalnus@schalnus.com
SOURCE: Ophthalmologica, (2003) 217/2 (89-98).
Refs: 154
ISSN: 0030-3755 CODEN: OPHTAD
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 012 Ophthalmology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Topically applied nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used in the management and prevention of ocular inflammation and cystoid macular edema related to cataract surgery and the maintenance of mydriasis during cataract surgery. Other common uses are the reduction of discomfort after refractive surgery or in allergic conjunctivitis. NSAIDs primarily act as cyclooxygenase inhibitors and thus reduce the formation of endogenous PGs. Today, several NSAIDs are commercially available: diclofenac, flurbiprofen, indomethacin, ketorolac and suprofen. At present the ophthalmologist has to make a decision between the use of topical corticosteroids, with their potential adverse effects, or of topical NSAIDs, with their possibly increased benefit, unknown effect on ocular pressure, wound healing and corneal tissue, higher costs and limited track record. However, the improvement of surgical techniques might support an increasing use of NSAIDs in the future. Preoperative anti-inflammatory treatment should be considered in eyes at a higher risk of developing severe postoperative inflammatory reactions. This decision has to be made carefully and has to be guided by the clinical circumstances, the spectrum of diagnosis and the individual benefit-risk ratio

of each patient.

CONTROLLED TERM: Medical Descriptors:
*eye inflammation: CO, complication
*eye inflammation: DM, disease management
*eye inflammation: DT, drug therapy
*eye inflammation: PC, prevention
*cataract: SU, surgery
*cataract extraction
antiinflammatory activity
topical treatment
ophthalmology
retina macula cystoid edema: CO, complication
retina macula cystoid edema: DT, drug therapy
mydriasis
allergic conjunctivitis: DT, drug therapy
drug mechanism
prostaglandin synthesis
side effect: SI, side effect
intraocular pressure
wound healing
cornea
drug cost
surgical technique
high risk population
disease severity
risk benefit analysis
drug indication
miosis: CO, complication
miosis: DT, drug therapy
miosis: PC, prevention
drug effect
blood eye barrier
drug efficacy
analytic method
drug formulation
food and drug administration
photophobia: CO, complication
photophobia: DT, drug therapy
postoperative pain: CO, complication
postoperative pain: DT, drug therapy
cornea injury: CO, complication
cornea injury: DT, drug therapy
papillary conjunctivitis: DT, drug therapy
burning sensation: SI, side effect
eye irritation: SI, side effect
conjunctival hyperemia: SI, side effect
anesthesia (sensory dysfunction): SI, side effect
cornea ulcer: SI, side effect
human
clinical trial
review
Drug Descriptors:
*nonsteroid antiinflammatory agent: CT, clinical trial
*nonsteroid antiinflammatory agent: AD, drug administration
*nonsteroid antiinflammatory agent: IT, drug interaction
*nonsteroid antiinflammatory agent: DT, drug therapy
*nonsteroid antiinflammatory agent: PE, pharmacoeconomics
*nonsteroid antiinflammatory agent: PD, pharmacology
*nonsteroid antiinflammatory agent: TP, topical drug administration
prostaglandin synthase inhibitor: CT, clinical trial
prostaglandin synthase inhibitor: AD, drug administration

prostaglandin synthase inhibitor: DT, drug therapy
prostaglandin synthase inhibitor: PR, pharmaceutics
prostaglandin synthase inhibitor: PD, pharmacology
prostaglandin synthase inhibitor: TP, topical drug administration
prostaglandin: EC, endogenous compound
diclofenac: CT, clinical trial
diclofenac: AD, drug administration
diclofenac: DT, drug therapy
diclofenac: PR, pharmaceutics
diclofenac: PD, pharmacology
diclofenac: TP, topical drug administration
flurbiprofen: CT, clinical trial
flurbiprofen: AD, drug administration
flurbiprofen: DT, drug therapy
flurbiprofen: PR, pharmaceutics
flurbiprofen: PD, pharmacology
flurbiprofen: TP, topical drug administration
indometacin: CT, clinical trial
indometacin: AD, drug administration
indometacin: DT, drug therapy
indometacin: PR, pharmaceutics
indometacin: PD, pharmacology
indometacin: TP, topical drug administration
ketorolac: CT, clinical trial
ketorolac: AD, drug administration
ketorolac: CM, drug comparison
ketorolac: DT, drug therapy
ketorolac: PR, pharmaceutics
ketorolac: PD, pharmacology
ketorolac: TP, topical drug administration
suprofen: AD, drug administration
suprofen: DT, drug therapy
suprofen: TP, topical drug administration
corticosteroid: AE, adverse drug reaction
corticosteroid: AD, drug administration
corticosteroid: CM, drug comparison
corticosteroid: IT, drug interaction
corticosteroid: DT, drug therapy
corticosteroid: PR, pharmaceutics
corticosteroid: PD, pharmacology
corticosteroid: TP, topical drug administration
ketorolac trometamol: CT, clinical trial
ketorolac trometamol: AD, drug administration
ketorolac trometamol: DT, drug therapy
ketorolac trometamol: PD, pharmacology
ketorolac trometamol: TP, topical drug administration
loteprednol etabonate: CT, clinical trial
loteprednol etabonate: CM, drug comparison
loteprednol etabonate: DT, drug therapy
loteprednol etabonate: PD, pharmacology
rimexolone: CM, drug comparison
rimexolone: DT, drug therapy
rimexolone: PD, pharmacology
dexamethasone: AD, drug administration
dexamethasone: CM, drug comparison
dexamethasone: DT, drug therapy
dexamethasone: PR, pharmaceutics
dexamethasone: PD, pharmacology
dexamethasone: TP, topical drug administration
prednisolone: AD, drug administration
prednisolone: CM, drug comparison
prednisolone: DT, drug therapy

prednisolone: PR, pharmaceutics
prednisolone: PD, pharmacology
prednisolone: TP, topical drug administration
levocabastine: CT, clinical trial
levocabastine: CM, drug comparison
levocabastine: DT, drug therapy
ocuflur
chibro ammuno

CAS REGISTRY NO.: (diclofenac) 15307-79-6, 15307-86-5; (flurbiprofen) 5104-49-4; (indometacin) 53-86-1, 74252-25-8, 7681-54-1; (ketorolac) 74103-06-3; (suprofen) 40828-46-4; (ketorolac trometamol) 74103-07-4; (loteprednol etabonate) 82034-46-6; (rimexolone) 49697-38-3; (dexamethasone) 50-02-2; (prednisolone) 50-24-8; (levocabastine) 79516-68-0

CHEMICAL NAME: Ocufen; Ocuflur; Profenal; Acular; Voltaren; Indoptol; Chibro ammuno

L86 ANSWER 7 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2003215859 EMBASE

TITLE: Hypersensitivity responses and contact lens wear.

AUTHOR: Stapleton F.; Stretton S.; Sankaridurg P.R.; Chandoha H.; Shovlin J.

CORPORATE SOURCE: F. Stapleton, Cornea/Contact Lens Research Unit, School of Optometry/Vision Science, University of New South Wales, Sydney, NSW 2052, Australia. f.stapleton@crcert.unsw.edu.au

SOURCE: Contact Lens and Anterior Eye, (2003) 26/2 (57-69).
Refs: 49
ISSN: 1367-0484 CODEN: CLAEAB

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 012 Ophthalmology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:
Hypersensitivity diseases that involve the eye are common reasons why patients present to eyecare practitioners. Common ocular hypersensitivity disorders include allergic conjunctivitis, giant or contact lens induced papillary conjunctivitis and atopic keratoconjunctivitis. The diagnosis and management of ocular hypersensitivity can present a challenge to eyecare practitioners and an understanding of the mechanisms that underlie the signs and symptoms of such conditions is necessary for their appropriate management. This article reviews the mechanisms by which the eye responds to antigenic challenges, the pathogenesis of ocular hypersensitivity responses, particularly in relation to contact lens wear, and illustrates possible management strategies. .COPYRGT. 2003 British Contact Lens Association. Published by Elsevier Science Ltd. All rights reserved.

CONTROLLED TERM: Medical Descriptors:
*hypersensitivity reaction: CO, complication
*hypersensitivity reaction: DI, diagnosis
*hypersensitivity reaction: DT, drug therapy
*hypersensitivity reaction: ET, etiology
*eye disease: CO, complication
*eye disease: DI, diagnosis
*eye disease: DT, drug therapy
*eye disease: ET, etiology
*contact lens
ophthalmology
medical specialist
allergic conjunctivitis: DI, diagnosis

papillary conjunctivitis: DI, diagnosis
keratoconjunctivitis: DI, diagnosis
symptomatology
retrospective study
pathogenesis
conjunctival hyperemia: SI, side effect
wound healing impairment: SI, side effect
headache: SI, side effect
rhinitis: SI, side effect
conjunctiva disease: SI, side effect
burning sensation: SI, side effect
cataract: SI, side effect
intraocular hypertension: SI, side effect
disease exacerbation: SI, side effect
superinfection: SI, side effect
human
review
priority journal
Drug Descriptors:
antigen
non prescription drug: AE, adverse drug reaction
non prescription drug: DT, drug therapy
non prescription drug: TP, topical drug administration
antihistaminic agent: AE, adverse drug reaction
antihistaminic agent: DT, drug therapy
antihistaminic agent: TP, topical drug administration
vasoconstrictor agent: AE, adverse drug reaction
vasoconstrictor agent: DT, drug therapy
vasoconstrictor agent: TP, topical drug administration
nonsteroid antiinflammatory agent: AE, adverse drug reaction
nonsteroid antiinflammatory agent: DT, drug therapy
nonsteroid antiinflammatory agent: PD, pharmacology
corticosteroid: AE, adverse drug reaction
corticosteroid: DT, drug therapy
corticosteroid: PD, pharmacology
corticosteroid: TP, topical drug administration
levocabastine: DT, drug therapy
levocabastine: TP, topical drug administration
emedastine: DT, drug therapy
emedastine: TP, topical drug administration
azelastine: DT, drug therapy
monoamine oxidase inhibitor
naphazoline: AE, adverse drug reaction
naphazoline: DT, drug therapy
pheniramine: AE, adverse drug reaction
pheniramine: DT, drug therapy
nedocromil sodium: DT, drug therapy
nedocromil sodium: PD, pharmacology
pemirolast: DT, drug therapy
pemirolast: PD, pharmacology
lodoxamide trometamol: DT, drug therapy
lodoxamide trometamol: PD, pharmacology
cromoglycate disodium: DT, drug therapy
cromoglycate disodium: PD, pharmacology
olopatadine: AE, adverse drug reaction
olopatadine: DT, drug therapy
olopatadine: PD, pharmacology
ketotifen fumarate: AE, adverse drug reaction
ketotifen fumarate: DT, drug therapy
ketotifen fumarate: PK, pharmacokinetics
ketotifen fumarate: PD, pharmacology
ketorolac trometamol: AE, adverse drug reaction

ketorolac trometamol: DT, drug therapy
ketorolac trometamol: PD, pharmacology
diclofenac: AE, adverse drug reaction
diclofenac: DT, drug therapy
diclofenac: PD, pharmacology
loteprednol etabonate: AE, adverse drug reaction
loteprednol etabonate: DT, drug therapy
loteprednol etabonate: PD, pharmacology
loteprednol etabonate: TP, topical drug administration
rimexolone: AE, adverse drug reaction
rimexolone: DT, drug therapy
rimexolone: PD, pharmacology
fluorometholone acetate: AE, adverse drug reaction
fluorometholone acetate: DT, drug therapy
fluorometholone acetate: PD, pharmacology
prednisolone acetate: AE, adverse drug reaction
prednisolone acetate: DT, drug therapy
prednisolone acetate: PD, pharmacology
unclassified drug
visine a
flarex

CAS REGISTRY NO.: (levocabastine) 79516-68-0; (emedastine) 87233-61-2, 87233-62-3; (azelastine) 58581-89-8, 79307-93-0; (naphazoline) 5144-52-5, 550-99-2, 835-31-4; (pheniramine) 86-21-5; (nedocromil sodium) 69049-74-7; (pemirolast) 69372-19-6; (lodoxamide trometamol) 63610-09-3; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (olopatadine) 113806-05-6, 140462-76-6; (ketotifen fumarate) 34580-14-8; (ketorolac trometamol) 74103-07-4; (diclofenac) 15307-79-6, 15307-86-5; (loteprednol etabonate) 82034-46-6; (rimexolone) 49697-38-3; (fluorometholone acetate) 3801-06-7; (prednisolone acetate) 52-21-1, 52628-64-5

CHEMICAL NAME: Pred forte; Flarex; Vexol; Lotemax; Alrex; Voltaren; Acular; Zaditor; Patanol; Crolom; Alomide; Alocril; Visine a; Naphcon a; Optivar; Emadine; Livostin

L86 ANSWER 8 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2003115353 EMBASE
TITLE: Olopatadine as first-line therapy in ocular allergy.
AUTHOR: Stoppel J.
CORPORATE SOURCE: Prof. J. Stoppel, University of Los Andes, Santiago, Chile
SOURCE: Clinical and Experimental Ophthalmology, (2003) 31/SUPPL. (S9-S12).
Refs: 10
ISSN: 1442-6404 CODEN: CEOPBW
COUNTRY: Australia
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 012 Ophthalmology
030 Pharmacology
038 Adverse Reactions Titles
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
***allergic conjunctivitis: DT, drug therapy**
human
clinical trial
nonhuman
mast cell

mast cell degranulation
histamine release
disease severity
patient compliance
drug efficacy
cell heterogeneity
tissue specificity
rabbit
drug effect
drug blood level
conjunctiva epithelium
neutrophil
cell infiltration
eosinophil
T lymphocyte activation
antiinflammatory activity
ocular pruritus: DT, drug therapy
statistical analysis
drug dose regimen
consultation
side effect: SI, side effect
drug safety
steady state
conference paper
Drug Descriptors:
*olopatadine: CM, drug comparison
*olopatadine: PD, pharmacology
*olopatadine: DT, drug therapy
*olopatadine: CT, clinical trial
*olopatadine: CR, drug concentration
*olopatadine: IO, intraocular drug administration
*olopatadine: AE, adverse drug reaction
antihistaminic agent: DT, drug therapy
antihistaminic agent: CB, drug combination
antihistaminic agent: CM, drug comparison
antihistaminic agent: CT, clinical trial
antihistaminic agent: PD, pharmacology
antihistaminic agent: CR, drug concentration
antihistaminic agent: IO, intraocular drug administration
antihistaminic agent: AE, adverse drug reaction
antihistaminic agent: PK, pharmacokinetics
nonsteroid antiinflammatory agent: DT, drug therapy
nonsteroid antiinflammatory agent: CB, drug combination
eotaxin: EC, endogenous compound
interleukin 8: EC, endogenous compound
RANTES: EC, endogenous compound
nedocromil sodium: CM, drug comparison
nedocromil sodium: PD, pharmacology
nedocromil sodium: DT, drug therapy
nedocromil sodium: CT, clinical trial
nedocromil sodium: CR, drug concentration
nedocromil sodium: IO, intraocular drug administration
nedocromil sodium: PK, pharmacokinetics
ketotifen fumarate: CT, clinical trial
ketotifen fumarate: CM, drug comparison
ketotifen fumarate: DT, drug therapy
ketotifen fumarate: PD, pharmacology
ketotifen fumarate: IO, intraocular drug administration
loteprednol etabonate: CT, clinical trial
loteprednol etabonate: DT, drug therapy
loteprednol etabonate: CM, drug comparison
loteprednol etabonate: CR, drug concentration
loteprednol etabonate: DO, drug dose

loteprednol etabonate: PD, pharmacology
loteprednol etabonate: IO, intraocular drug administration
emedastine: CM, drug comparison
emedastine: DT, drug therapy
emedastine: PD, pharmacology
levocabastine: CM, drug comparison
levocabastine: DT, drug therapy
levocabastine: PD, pharmacology
tumor necrosis factor alpha: EC, endogenous compound
interleukin 4: EC, endogenous compound
interleukin 13: EC, endogenous compound
mast cell stabilizer: DT, drug therapy
mast cell stabilizer: CB, drug combination
mast cell stabilizer: CM, drug comparison
mast cell stabilizer: PD, pharmacology
mast cell stabilizer: CT, clinical trial
mast cell stabilizer: CR, drug concentration
mast cell stabilizer: IO, intraocular drug administration
mast cell stabilizer: AE, adverse drug reaction
antiallergic agent: DT, drug therapy
antiallergic agent: CB, drug combination
antiallergic agent: CM, drug comparison
antiallergic agent: PD, pharmacology
antiallergic agent: CT, clinical trial
antiallergic agent: CR, drug concentration
antiallergic agent: IO, intraocular drug administration
antiallergic agent: AE, adverse drug reaction
antiallergic agent: PK, pharmacokinetics
histamine H1 receptor: EC, endogenous compound
antazoline: DT, drug therapy
antazoline: PD, pharmacology
antazoline: CM, drug comparison
pheniramine: DT, drug therapy
pheniramine: PD, pharmacology
pheniramine: CM, drug comparison
histamine H1 receptor antagonist: DT, drug therapy
histamine H1 receptor antagonist: CB, drug combination
histamine H1 receptor antagonist: CM, drug comparison
histamine H1 receptor antagonist: CT, clinical trial
histamine H1 receptor antagonist: PD, pharmacology
histamine H1 receptor antagonist: CR, drug concentration
histamine H1 receptor antagonist: IO, intraocular drug administration
placebo
unclassified drug

CAS REGISTRY NO.: (olopatadine) 113806-05-6, 140462-76-6; (interleukin 8) 114308-91-7; (nedocromil sodium) 69049-74-7; (ketotifen fumarate) 34580-14-8; (loteprednol etabonate) 82034-46-6; (emedastine) 87233-61-2, 87233-62-3; (levocabastine) 79516-68-0; (interleukin 13) 148157-34-0; (antazoline) 154-68-7, 2508-72-7, 3131-32-6, 91-75-8; (pheniramine) 86-21-5

CHEMICAL NAME: Patanol; Alocril; Alrex; Zaditor

L86 ANSWER 9 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002177109 EMBASE
TITLE: Update on ocular allergy treatment.
AUTHOR: Bielory L.
CORPORATE SOURCE: Dr. L. Bielory, UMDNJ - Asthma/Allergy Res. Center, Department of Medicine, New Jersey Medical School, Newark, NJ 07103, United States. bielory@umdnj.edu

SOURCE: Expert Opinion on Pharmacotherapy, (2002) 3/5 (541-553).
Refs: 115
ISSN: 1465-6566 CODEN: EOPHF7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 012 Ophthalmology
030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT:
Allergy affects > 15% of the world population with a higher prevalence of 30% in westernised industrialised countries, such as the US. Allergy commonly affects various target organs including the eyes, nose, sinuses, ears, lungs and skin. However, the ocular component may be the most common and initially the most prominent disabling feature. Some patients are affected for only a few weeks to months while others have symptoms that last throughout the year. The associated healthcare costs related to allergic conjunctivitis has been commonly nestled with allergic rhinitis and has been reported to be as high as US$5.9 billion in the US, with 25% (US$1.5 billion) of it related to medication use. The expenditures related to ocular prescription medication has only recently risen in the past decade from US$6 million in early 1990s to > US$200 million in the new millennium with a projected continuous expansion of 25% per year. This appears to be due to improved prescription medications and their clear benefit over the less efficacious over-the-counter products. The actual cost of the medications and their relative price increases over the past year have ranged from 0-49% with an average cost of < US$ day. The newer topical medications (multiple acting agents) are focusing on multiple actions that include an antihistaminic effect to provide an immediate relief and additional delayed effects to act on the mediators of the late phase reaction without steroid side effects (glaucoma, cataracts). The paradigm for the treatment of ocular allergy ranges from primary measures (avoidance measures, cold compresses and lubrication), to secondary measures (various combination of topical agents) and tertiary measures that would include topical steroids and immunotherapy. The increased interest in advancing ocular treatment will lead to the development of additional therapies, novel pharmacokinetic delivery systems and, thus, improved healthcare outcomes for patients with allergic conjunctivitis.

CONTROLLED TERM: Medical Descriptors:
***allergic conjunctivitis: DM, disease management**
***allergic conjunctivitis: DT, drug therapy**
***allergic conjunctivitis: TH, therapy**
prevalence
Western Hemisphere
industrialization
United States
target organ
nose allergy
ear disease
respiratory tract allergy
skin allergy
disease duration
symptomatology
health care cost
allergic rhinitis
drug use
prescription
drug efficacy
drug cost

glaucoma: SI, side effect
cataract: SI, side effect
avoidance behavior
cold treatment
lubrication
immunotherapy
drug delivery system
drug formulation
heat sensation
hyperemia: SI, side effect
drug absorption
drug potentiation
dry eye: SI, side effect
drug blood level
human
controlled study
child
adult
review
Drug Descriptors:
non prescription drug: DT, drug therapy
non prescription drug: PD, pharmacology
topical agent: AE, adverse drug reaction
topical agent: CB, drug combination
topical agent: DT, drug therapy
topical agent: PE, pharmacoeconomics
topical agent: PK, pharmacokinetics
topical agent: PD, pharmacology
topical agent: TP, topical drug administration
steroid: AE, adverse drug reaction
steroid: DT, drug therapy
steroid: TP, topical drug administration
artificial tear: DT, drug therapy
artificial tear: PR, pharmaceutics
artificial tear: PD, pharmacology
artificial tear: TP, topical drug administration
decongestive agent: AE, adverse drug reaction
decongestive agent: CB, drug combination
decongestive agent: IT, drug interaction
decongestive agent: DT, drug therapy
decongestive agent: PK, pharmacokinetics
decongestive agent: PD, pharmacology
decongestive agent: TP, topical drug administration
phenylephrine: AE, adverse drug reaction
phenylephrine: CB, drug combination
phenylephrine: DT, drug therapy
phenylephrine: PK, pharmacokinetics
phenylephrine: PD, pharmacology
phenylephrine: TP, topical drug administration
tetryzoline: AE, adverse drug reaction
tetryzoline: CB, drug combination
tetryzoline: DT, drug therapy
tetryzoline: PK, pharmacokinetics
tetryzoline: PD, pharmacology
tetryzoline: TP, topical drug administration
antazoline: CB, drug combination
antazoline: CM, drug comparison
antazoline: DT, drug therapy
antazoline: PD, pharmacology
antazoline: TP, topical drug administration
naphazoline: CB, drug combination
naphazoline: DT, drug therapy
naphazoline: PD, pharmacology

naphazoline: TP, topical drug administration
pheniramine: CB, drug combination
pheniramine: CM, drug comparison
pheniramine: DT, drug therapy
pheniramine: PD, pharmacology
pheniramine: TP, topical drug administration
histamine H1 receptor antagonist: AE, adverse drug reaction
histamine H1 receptor antagonist: CB, drug combination
histamine H1 receptor antagonist: IT, drug interaction
histamine H1 receptor antagonist: DT, drug therapy
histamine H1 receptor antagonist: PD, pharmacology
histamine H1 receptor antagonist: PO, oral drug administration
histamine H1 receptor antagonist: TP, topical drug administration
olopatadine: CM, drug comparison
olopatadine: DT, drug therapy
olopatadine: PR, pharmaceutics
olopatadine: PD, pharmacology
olopatadine: TP, topical drug administration
ketotifen fumarate: AE, adverse drug reaction
ketotifen fumarate: CM, drug comparison
ketotifen fumarate: DT, drug therapy
ketotifen fumarate: PR, pharmaceutics
ketotifen fumarate: PD, pharmacology
ketotifen fumarate: PO, oral drug administration
ketotifen fumarate: TP, topical drug administration
azelastine: CM, drug comparison
azelastine: DT, drug therapy
azelastine: PR, pharmaceutics
azelastine: PD, pharmacology
azelastine: NA, intranasal drug administration
azelastine: PO, oral drug administration
azelastine: TP, topical drug administration
cromoglycate disodium: AE, adverse drug reaction
cromoglycate disodium: CM, drug comparison
cromoglycate disodium: DT, drug therapy
cromoglycate disodium: PR, pharmaceutics
cromoglycate disodium: PD, pharmacology
cromoglycate disodium: TP, topical drug administration
lodoxamide trometamol: CM, drug comparison
lodoxamide trometamol: DT, drug therapy
lodoxamide trometamol: PR, pharmaceutics
lodoxamide trometamol: PD, pharmacology
lodoxamide trometamol: TP, topical drug administration
nedocromil sodium: CM, drug comparison
nedocromil sodium: DT, drug therapy
nedocromil sodium: PR, pharmaceutics
nedocromil sodium: PD, pharmacology
nedocromil sodium: TP, topical drug administration
pemirolast: AE, adverse drug reaction
pemirolast: CM, drug comparison
pemirolast: DT, drug therapy
pemirolast: PR, pharmaceutics
pemirolast: PD, pharmacology
pemirolast: TP, topical drug administration
levocabastine: CM, drug comparison
levocabastine: CR, drug concentration
levocabastine: DT, drug therapy
levocabastine: PR, pharmaceutics
levocabastine: PK, pharmacokinetics
levocabastine: PD, pharmacology
levocabastine: TP, topical drug administration

emedastine: CM, drug comparison
emedastine: CR, drug concentration
emedastine: DT, drug therapy
emedastine: PR, pharmaceutics
emedastine: PK, pharmacokinetics
emedastine: PD, pharmacology
emedastine: TP, topical drug administration
ketorolac trometamol: CM, drug comparison
ketorolac trometamol: DT, drug therapy
ketorolac trometamol: PR, pharmaceutics
ketorolac trometamol: PD, pharmacology
ketorolac trometamol: TP, topical drug administration
loteprednol etabonate: AE, adverse drug reaction
loteprednol etabonate: CM, drug comparison
loteprednol etabonate: DT, drug therapy
loteprednol etabonate: PR, pharmaceutics
loteprednol etabonate: PD, pharmacology
loteprednol etabonate: TP, topical drug administration
rimexolone: DT, drug therapy
rimexolone: PD, pharmacology
rimexolone: TP, topical drug administration
fluorometholone: DT, drug therapy
fluorometholone: PD, pharmacology
fluorometholone: TP, topical drug administration
loratadine: DT, drug therapy
loratadine: PD, pharmacology
loratadine: TP, topical drug administration
fexofenadine: DT, drug therapy
fexofenadine: PD, pharmacology
fexofenadine: TP, topical drug administration
cetirizine: DT, drug therapy
cetirizine: PD, pharmacology
cetirizine: TP, topical drug administration
nonsteroid antiinflammatory agent: CM, drug comparison
nonsteroid antiinflammatory agent: DT, drug therapy
nonsteroid antiinflammatory agent: PR, pharmaceutics
nonsteroid antiinflammatory agent: PD, pharmacology
nonsteroid antiinflammatory agent: PO, oral drug administration
nonsteroid antiinflammatory agent: TP, topical drug administration
flurbiprofen: DT, drug therapy
flurbiprofen: PR, pharmaceutics
flurbiprofen: PD, pharmacology
flurbiprofen: TP, topical drug administration
unindexed drug
fml
genteal

CAS REGISTRY NO.: (phenylephrine) 532-38-7, 59-42-7, 61-76-7; (tetryzoline) 522-48-5, 84-22-0; (antazoline) 154-68-7, 2508-72-7, 3131-32-6, 91-75-8; (naphazoline) 5144-52-5, 550-99-2, 835-31-4; (pheniramine) 86-21-5; (olopatadine) 113806-05-6, 140462-76-6; (ketotifen fumarate) 34580-14-8; (azelastine) 58581-89-8, 79307-93-0; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (lodoxamide trometamol) 63610-09-3; (nedocromil sodium) 69049-74-7; (pemirolast) 69372-19-6; (levocabastine) 79516-68-0; (emedastine) 87233-61-2, 87233-62-3; (ketorolac trometamol) 74103-07-4; (loteprednol etabonate) 82034-46-6; (rimexolone) 49697-38-3; (fluorometholone) 426-13-1; (loratadine) 79794-75-5; (fexofenadine) 138452-21-8; (cetirizine) 83881-51-0, 83881-52-1; (flurbiprofen) 5104-49-4

CHEMICAL NAME: (1) Patanol; (2) Zaditor; (3) Optivar; (4) Alocril; (5) Emadine; (6) Acular; (7) Alrex; Crolom; Alomide; Alamast; Livostin; Lotemax; Vexol; Fml; Genteal; Opticrom; Ocufen
COMPANY NAME: (2) Ciba Vision; (3) Muro; (5) Alcon; (6) Allergan; (7) Bausch and Lomb

L86 ANSWER 10 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002375915 EMBASE
TITLE: Progress in the pharmacotherapeutics of allergic conjunctivitis.
AUTHOR: Chen Z.
CORPORATE SOURCE: Z. Chen, Henan Institute of Ophthalmology, Zhengzhou 450003, China
SOURCE: Chinese Ophthalmic Research, (2002) 20/5 (475-478).
Refs: 29
ISSN: 1003-0808 CODEN: YAYAFH
COUNTRY: China
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 012 Ophthalmology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: Chinese
SUMMARY LANGUAGE: English; Chinese
ABSTRACT:
The pathogenesis of allergic conjunctivitis involves multiple mechanisms. Along with the intensive explore for the pathogenic mechanisms, the significant progress have been achieved in the pharmacotherapeutics, newer drugs have been discovered continuously. These new drugs in the ocular topically used include histamine H(1) blockers (ketotifen, levocabastine, emedastine, olopatadine, azelastine, mequitazine). mast cell stabilizers (nedocromil, lodoxamide, pemirolast), glucocorticoids rimexolone, loteprednol) and immunosuppression agents (cyclospoline A, tacrolimus). This article is to present in detail for pharmacological effect, mechanism of action, clinical efficacy and adverse effect of these new drugs.

CONTROLLED TERM: Medical Descriptors:
***allergic conjunctivitis: DT, drug therapy**
***allergic conjunctivitis: ET, etiology**
pathogenesis
drug effect
drug mechanism
drug efficacy
side effect: SI, side effect
human
review
Drug Descriptors:
*histamine H1 receptor antagonist: AE, adverse drug reaction
*histamine H1 receptor antagonist: DT, drug therapy
*histamine H1 receptor antagonist: PD, pharmacology
*histamine H1 receptor antagonist: TP, topical drug administration
*glucocorticoid: AE, adverse drug reaction
*glucocorticoid: DT, drug therapy
*glucocorticoid: PD, pharmacology
*glucocorticoid: TP, topical drug administration
*immunosuppressive agent: AE, adverse drug reaction
*immunosuppressive agent: DT, drug therapy
*immunosuppressive agent: PD, pharmacology
*immunosuppressive agent: TP, topical drug administration
new drug: AE, adverse drug reaction
new drug: DT, drug therapy

new drug: PD, pharmacology
new drug: TP, topical drug administration
ketotifen fumarate: AE, adverse drug reaction
ketotifen fumarate: DT, drug therapy
ketotifen fumarate: PD, pharmacology
ketotifen fumarate: TP, topical drug administration
levocabastine: AE, adverse drug reaction
levocabastine: DT, drug therapy
levocabastine: PD, pharmacology
levocabastine: TP, topical drug administration
emedastine: AE, adverse drug reaction
emedastine: DT, drug therapy
emedastine: PD, pharmacology
emedastine: TP, topical drug administration
olopatadine: AE, adverse drug reaction
olopatadine: DT, drug therapy
olopatadine: PD, pharmacology
olopatadine: TP, topical drug administration
azelastine: AE, adverse drug reaction
azelastine: DT, drug therapy
azelastine: PD, pharmacology
azelastine: TP, topical drug administration
mequitazine: AE, adverse drug reaction
mequitazine: DT, drug therapy
mequitazine: PD, pharmacology
mequitazine: TP, topical drug administration
nedocromil: AE, adverse drug reaction
nedocromil: DT, drug therapy
nedocromil: PD, pharmacology
nedocromil: TP, topical drug administration
pemirolast: AE, adverse drug reaction
pemirolast: DT, drug therapy
pemirolast: PD, pharmacology
pemirolast: TP, topical drug administration
rimexolone: AE, adverse drug reaction
rimexolone: DT, drug therapy
rimexolone: PD, pharmacology
rimexolone: TP, topical drug administration
loteprednol etabonate: AE, adverse drug reaction
loteprednol etabonate: DT, drug therapy
loteprednol etabonate: PD, pharmacology
loteprednol etabonate: TP, topical drug administration
cyclosporin A: AE, adverse drug reaction
cyclosporin A: DT, drug therapy
cyclosporin A: PD, pharmacology
cyclosporin A: TP, topical drug administration
tsukubaenolide: AE, adverse drug reaction
tsukubaenolide: DT, drug therapy
tsukubaenolide: PD, pharmacology
tsukubaenolide: TP, topical drug administration
lodoxamide trometamol: AE, adverse drug reaction
lodoxamide trometamol: DT, drug therapy
lodoxamide trometamol: PD, pharmacology
lodoxamide trometamol: TP, topical drug administration
levocarbinoxamine

CAS REGISTRY NO.: (ketotifen fumarate) 34580-14-8; (levocabastine) 79516-68-0; (emedastine) 87233-61-2, 87233-62-3; (olopatadine) 113806-05-6, 140462-76-6; (azelastine) 58581-89-8, 79307-93-0; (mequitazine) 29216-28-2; (nedocromil) 69049-73-6; (pemirolast) 69372-19-6; (rimexolone) 49697-38-3; (loteprednol etabonate) 82034-46-6; (cyclosporin A) 59865-13-3, 63798-73-2;

(tsukubaenolide) 104987-11-3; (lodoxamide trometamol) 63610-09-3
CHEMICAL NAME: Zaditen; Zasten; Livostin; Levocarbinoxamine; Emadine; Patanol; Azeptin; Astelin; Primalan; Alomide; Fk 506

L86 ANSWER 11 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001088023 EMBASE
TITLE: Current therapy of ocular allergy.
AUTHOR: Friedlaender M.H.
CORPORATE SOURCE: Prof. M.H. Friedlaender, Scripps Clinic, Division of Ophthalmology, MS214, 10666 North Torrey Pines Road, San Diego, CA 92037, United States
SOURCE: Today's Therapeutic Trends, (2001) 19/1 (23-37).
Refs: 37
ISSN: 0741-2320 CODEN: TTTRDH
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 012 Ophthalmology
030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Ocular allergy (allergic conjunctivitis) can vary significantly in both its clinical presentation and severity of the condition. Seasonal allergic conjunctivitis (SAC), which accounts for more than half of all cases, is characterized by early onset (generally before the age of 30), a strong family history of allergy prominent itching and recurrent episodes. Combination vasoconstrictor/antihistamine eyedrops have been widely used to treat ocular allergy, and are generally safe, efficacious and cost-effective. Antihistamines, which act by blocking the H(1) histamine receptor, are highly effective in providing relief of itching but are not very active in relieving the associated redness. Newer antiallergic eyedrops, including ketotifen, nedocromil and pemirolast, provide a combination of anti-inflammatory, mast-cell stabilizing and anti-histamine effects. Another new agent with such multiple mechanisms of action, azelastine hydrochloride (Optivar.RTM.), was recently shown in a placebo-controlled trial to statistically significantly reduce itching and conjunctival redness, as well as mean tearing and chemosis scores. Azelastine ophthalmic solution provided significant long-term benefit in relieving the symptoms of allergic conjunctivitis, with a duration of action of at least 10 hours for itching and redness, and was well tolerated. New corticosteroid agents that are associated with fewer side effects than traditional steroidal preparations have also been developed in eyedrop form for use in treating ocular allergy.

CONTROLLED TERM: Medical Descriptors:
*eye disease: DI, diagnosis
*eye disease: DM, disease management
*eye disease: DT, drug therapy
*eye disease: ET, etiology
*eye disease: TH, therapy
***allergy: DI, diagnosis**
***allergy: DM, disease management**
***allergy: DT, drug therapy**
***allergy: ET, etiology**
***allergy: TH, therapy**
clinical feature
disease severity
allergic conjunctivitis: DI, diagnosis
allergic conjunctivitis: DM, disease management
allergic conjunctivitis: DT, drug therapy

Searched by Barb O'Bryen, STIC 308-4291

allergic conjunctivitis: ET, etiology
allergic conjunctivitis: TH, therapy
onset age
family history
pruritus
drug safety
drug efficacy
cost effectiveness analysis
drug effect
side effect: SI, side effect
papillary conjunctivitis: DI, diagnosis
papillary conjunctivitis: DT, drug therapy
papillary conjunctivitis: ET, etiology
papillary conjunctivitis: TH, therapy
keratoconjunctivitis: DI, diagnosis
keratoconjunctivitis: DT, drug therapy
keratoconjunctivitis: ET, etiology
keratoconjunctivitis: TH, therapy
disease classification
treatment outcome
drug mechanism
human
nonhuman
review
Drug Descriptors:
*eye drops: AE, adverse drug reaction
*eye drops: CB, drug combination
*eye drops: DT, drug therapy
*eye drops: PE, pharmacoeconomics
*eye drops: PD, pharmacology
*eye drops: TP, topical drug administration
***antiallergic agent: AE, adverse drug reaction**
***antiallergic agent: CB, drug combination**
***antiallergic agent: DT, drug therapy**
***antiallergic agent: PE, pharmacoeconomics**
***antiallergic agent: PD, pharmacology**
***antiallergic agent: TP, topical drug administration**
ketotifen: DT, drug therapy
ketotifen: PD, pharmacology
ketotifen: TP, topical drug administration
nedocromil: DT, drug therapy
nedocromil: PD, pharmacology
nedocromil: TP, topical drug administration
pemirolast: DT, drug therapy
pemirolast: PD, pharmacology
pemirolast: TP, topical drug administration
azelastine: DT, drug therapy
azelastine: PD, pharmacology
azelastine: TP, topical drug administration
corticosteroid: AE, adverse drug reaction
corticosteroid: DT, drug therapy
corticosteroid: PD, pharmacology
corticosteroid: TP, topical drug administration
vasoconstrictor agent: CB, drug combination
vasoconstrictor agent: DT, drug therapy
vasoconstrictor agent: PE, pharmacoeconomics
vasoconstrictor agent: TP, topical drug administration
naphazoline: CB, drug combination
naphazoline: DT, drug therapy
naphazoline: TP, topical drug administration
antazoline: CB, drug combination
antazoline: DT, drug therapy

antazoline: TP, topical drug administration
pheniramine: CB, drug combination
pheniramine: DT, drug therapy
pheniramine: TP, topical drug administration
histamine H1 receptor antagonist: CB, drug combination
histamine H1 receptor antagonist: DT, drug therapy
histamine H1 receptor antagonist: PE, pharmacoeconomics
histamine H1 receptor antagonist: PD, pharmacology
histamine H1 receptor antagonist: TP, topical drug administration
levocabastine: DT, drug therapy
levocabastine: TP, topical drug administration
emedastine: DT, drug therapy
emedastine: TP, topical drug administration
cromoglycate disodium: DT, drug therapy
cromoglycate disodium: TP, topical drug administration
lodoxamide: DT, drug therapy
lodoxamide: PD, pharmacology
lodoxamide: TP, topical drug administration
olopatadine: DT, drug therapy
olopatadine: PD, pharmacology
olopatadine: TP, topical drug administration
nonsteroid antiinflammatory agent: DT, drug therapy
nonsteroid antiinflammatory agent: PD, pharmacology
nonsteroid antiinflammatory agent: TP, topical drug administration
ketorolac trometamol: DT, drug therapy
ketorolac trometamol: PD, pharmacology
ketorolac trometamol: TP, topical drug administration
loteprednol etabonate: AE, adverse drug reaction
loteprednol etabonate: DT, drug therapy
loteprednol etabonate: PD, pharmacology
loteprednol etabonate: TP, topical drug administration
rimexolone: DT, drug therapy
fluorometholone: DT, drug therapy
optivar
lodoxamide trometamol
ketotifen fumarate
nedocromil sodium
fml
fluor op

CAS REGISTRY NO.: (ketotifen) 34580-13-7; (nedocromil) 69049-73-6; (pemirolast) 69372-19-6; (azelastine) 58581-89-8, 79307-93-0; (naphazoline) 5144-52-5, 550-99-2, 835-31-4; (antazoline) 154-68-7, 2508-72-7, 3131-32-6, 91-75-8; (pheniramine) 86-21-5; (levocabastine) 79516-68-0; (emedastine) 87233-61-2, 87233-62-3; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (lodoxamide) 53882-12-5; (olopatadine) 113806-05-6, 140462-76-6; (ketorolac trometamol) 74103-07-4; (loteprednol etabonate) 82034-46-6; (rimexolone) 49697-38-3; (fluorometholone) 426-13-1; (lodoxamide trometamol) 63610-09-3; (ketotifen fumarate) 34580-14-8; (nedocromil sodium) 69049-74-7

CHEMICAL NAME: Optivar; Alomide; Patanol; Zaditor; Alocril; Alamast; Acular; Lotemax; Alrex; Vexol; Fml; Fluor op

L86 ANSWER 12 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000427682 EMBASE
TITLE: Allergic conjunctivitis; Bacterial conjunctivitis; Chlamydial conjunctivitis in the adult (Adult inclusion conjunctivitis); Adenoviral infections.

Searched by Barb O'Bryen, STIC 308-4291

SOURCE: Practical Optometry, (2000) 11/5 (182-188).
ISSN: 1181-6058 CODEN: PROPFW
COUNTRY: Canada
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
012 Ophthalmology
027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
***allergic conjunctivitis: DI, diagnosis**
***allergic conjunctivitis: DT, drug therapy**
*conjunctivitis: DI, diagnosis
*conjunctivitis: DT, drug therapy
*chlamydiasis: DI, diagnosis
*chlamydiasis: DT, drug therapy
*virus infection: DI, diagnosis
*virus infection: DT, drug therapy
*virus infection: TH, therapy
*pharyngoconjunctival fever: DI, diagnosis
*pharyngoconjunctival fever: DT, drug therapy
pruritus: DT, drug therapy
hyperemia
Adenovirus
compression therapy
lymphadenopathy
upper respiratory tract infection
sore throat
human
female
clinical article
child
adult
review
Drug Descriptors:
*ketotifen fumarate: DT, drug therapy
*ketotifen fumarate: TP, topical drug administration
*tobramycin: DT, drug therapy
*tobramycin: TP, topical drug administration
*azithromycin: DT, drug therapy
*azithromycin: PO, oral drug administration
***loteprednol etabonate: DT, drug therapy**
*artificial tear
naphazoline: DT, drug therapy
naphazoline: TP, topical drug administration
pheniramine maleate: DT, drug therapy
pheniramine maleate: TP, topical drug administration
levocabastine: TP, topical drug administration
emedastine: TP, topical drug administration
olopatadine: TP, topical drug administration
azelastine: TP, topical drug administration
antazoline: TP, topical drug administration
lodoxamide trometamol: TP, topical drug administration
cromoglycate disodium: TP, topical drug administration
nedocromil sodium: TP, topical drug administration
pemirolast: TP, topical drug administration
ketorolac: TP, topical drug administration
diclofenac: TP, topical drug administration
antihistaminic agent: TP, topical drug administration
decongestive agent: TP, topical drug administration
nonsteroid antiinflammatory agent: TP, topical drug

administration
optivar
vasocon a
visine a
alamast
ketorolac trometamol

CAS REGISTRY NO.: (ketotifen fumarate) 34580-14-8; (tobramycin) 32986-56-4; (azithromycin) 83905-01-5; (loteprednol etabonate) 82034-46-6; (naphazoline) 5144-52-5, 550-99-2, 835-31-4; (pheniramine maleate) 132-20-7; (levocabastine) 79516-68-0; (emedastine) 87233-61-2, 87233-62-3; (olopatadine) 113806-05-6, 140462-76-6; (azelastine) 58581-89-8, 79307-93-0; (antazoline) 154-68-7, 2508-72-7, 3131-32-6, 91-75-8; (lodoxamide trometamol) 63610-09-3; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (nedocromil sodium) 69049-74-7; (pemirolast) 69372-19-6; (ketorolac) 74103-06-3; (diclofenac) 15307-79-6, 15307-86-5; (vasocon a) 60747-34-4; (ketorolac trometamol) 74103-07-4

CHEMICAL NAME: Zaditen; Zithromax; Livostin; Emadine; Patanol; Optivar; Vasocon a; Naphcon a; Visine a; Alomide; Crolom; Opticrom; Alocril; Alamast; Acular; Voltaren; Lotemax; Alrex

NAME OF PRODUCT: GenTeal gel

L86 ANSWER 13 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000337735 EMBASE

TITLE: Ocular allergic disorders and dry eye disease: Associations, diagnostic dilemmas, and management.

AUTHOR: Berdy G.J.; Hedqvist B.

CORPORATE SOURCE: G.J. Berdy, Clin. Inst. in Ophthal., Washington Univ. of Sch. of Medicine, St. Louis, MO, United States

SOURCE: Acta Ophthalmologica Scandinavica, Supplement, (2000) 78/230 (32-37).
Refs: 84
ISSN: 1395-3931 CODEN: AOSSFB

COUNTRY: Denmark

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index

LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
*eye disease: DI, diagnosis
*eye disease: DT, drug therapy
***allergy: DI, diagnosis**
***allergy: DT, drug therapy**
*dry eye: DI, diagnosis
*dry eye: DT, drug therapy
clinical feature
keratoconjunctivitis sicca: DI, diagnosis
keratoconjunctivitis sicca: DT, drug therapy
allergic conjunctivitis: DI, diagnosis
allergic conjunctivitis: DT, drug therapy
hypersensitivity: DI, diagnosis
hypersensitivity: DT, drug therapy
tear film
human
review
priority journal
Drug Descriptors:
oxymetazoline: DT, drug therapy
oxymetazoline: TP, topical drug administration
tetryzoline: DT, drug therapy

Searched by Barb O'Bryen, STIC 308-4291

tetryzoline: TP, topical drug administration
ocular antiinflammatory agent: DT, drug therapy
naphazoline: DT, drug therapy
emedastine: DT, drug therapy
levocabastine: DT, drug therapy
lodoxamide trometamol: DT, drug therapy
cromoglycate disodium: DT, drug therapy
olopatadine: DT, drug therapy
ketotifen: DT, drug therapy
nonsteroid antiinflammatory agent: DT, drug therapy
nonsteroid antiinflammatory agent: TP, topical drug administration
ketorolac trometamol: DT, drug therapy
loteprednol etabonate: DT, drug therapy
antihistaminic agent: DT, drug therapy
antihistaminic agent: PO, oral drug administration
loratadine: DT, drug therapy
loratadine: PO, oral drug administration
fexofenadine: DT, drug therapy
cetirizine: DT, drug therapy
cetirizine: PO, oral drug administration
fluorescein
artificial tear: DT, drug therapy
doxycycline: PO, oral drug administration
zaditor
murine

CAS REGISTRY NO.: (oxymetazoline) 1491-59-4, 2315-02-8; (tetryzoline) 522-48-5, 84-22-0; (naphazoline) 5144-52-5, 550-99-2, 835-31-4; (emedastine) 87233-61-2, 87233-62-3; (levocabastine) 79516-68-0; (lodoxamide trometamol) 63610-09-3; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (olopatadine) 113806-05-6, 140462-76-6; (ketotifen) 34580-13-7; (ketorolac trometamol) 74103-07-4; (loteprednol etabonate) 82034-46-6; (loratadine) 79794-75-5; (fexofenadine) 138452-21-8; (cetirizine) 83881-51-0, 83881-52-1; (fluorescein) 2321-07-5, 91316-42-6; (doxycycline) 10592-13-9, 17086-28-1, 564-25-0

CHEMICAL NAME: Claritin; Allegra; Zyrtec; Zaditor; Patanol; Crolom; Emadine; Livostin; Murine; Visine; Afrin

L86 ANSWER 14 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999418382 EMBASE
TITLE: Ocular allergies: Clinical diagnosis and management.
AUTHOR: Hansen D.W.
CORPORATE SOURCE: Dr. D.W. Hansen, 2600 Grand Avenue, Des Moines, IA 50312-5300, United States
SOURCE: Practical Optometry, (1999) 10/5 (194-202).
Refs: 5
ISSN: 1181-6058 CODEN: PROPFW
COUNTRY: Canada
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Ocular allergies are a common optometric clinical presentation. Environmental elements, chemicals, and drugs can induce ocular allergies. This paper discusses the clinical diagnosis and management of ocular allergies. Emphasis is placed on medical treatment, including the use of pharmaceutical agents.

CONTROLLED TERM: Medical Descriptors:
*eye disease: DI, diagnosis
*eye disease: DT, drug therapy
*eye disease: ET, etiology
***allergy: DI, diagnosis**
***allergy: DT, drug therapy**
***allergy: ET, etiology**
allergic conjunctivitis: DI, diagnosis
allergic conjunctivitis: DT, drug therapy
allergic conjunctivitis: ET, etiology
contact allergy: DI, diagnosis
contact allergy: DT, drug therapy
contact allergy: ET, etiology
vernal conjunctivitis: DI, diagnosis
vernal conjunctivitis: DT, drug therapy
vernal conjunctivitis: ET, etiology
keratoconjunctivitis: DI, diagnosis
keratoconjunctivitis: DT, drug therapy
keratoconjunctivitis: ET, etiology
symptomatology
allergic reaction
inflammation
eosinophil
environmental factor
genetic predisposition
allergy test
intraocular hypertension: SI, side effect
cataract: SI, side effect
drowsiness: SI, side effect
cardiotoxicity: SI, side effect
pruritus: DT, drug therapy
hyperemia: DT, drug therapy
eye infection: CO, complication
eye infection: DT, drug therapy
human
oral drug administration
topical drug administration
article
Drug Descriptors:
*antihistaminic agent: DT, drug therapy
*antihistaminic agent: PD, pharmacology
*nonsteroid antiinflammatory agent: DT, drug therapy
*corticosteroid: AE, adverse drug reaction
*corticosteroid: DT, drug therapy
*homeopathic agent: DT, drug therapy
*artificial tear: DT, drug therapy
*antibiotic agent: DT, drug therapy
levocabastine: DT, drug therapy
levocabastine: PD, pharmacology
emedastine: DT, drug therapy
emedastine: PD, pharmacology
olopatadine: DT, drug therapy
ketorolac trometamol: DT, drug therapy
loteprednol etabonate: DT, drug therapy
rimexolone: DT, drug therapy
chlorpheniramine: AE, adverse drug reaction
chlorpheniramine: DT, drug therapy
loratadine: DT, drug therapy
cetirizine: DT, drug therapy
terfenadine: AE, adverse drug reaction
terfenadine: IT, drug interaction
terfenadine: DT, drug therapy
astemizole: AE, adverse drug reaction

astemizole: IT, drug interaction
astemizole: DT, drug therapy
cyclosporin: AE, adverse drug reaction
cyclosporin: IT, drug interaction
phenytoin: AE, adverse drug reaction
phenytoin: IT, drug interaction
antifungal agent: AE, adverse drug reaction
antifungal agent: IT, drug interaction
similasan: DT, drug therapy
fluorometholone: DT, drug therapy
tetracycline: DT, drug therapy
doxycycline: DT, drug therapy
emadine
alrex
flarex

CAS REGISTRY NO.: (levocabastine) 79516-68-0; (emedastine) 87233-61-2, 87233-62-3; (olopatadine) 113806-05-6, 140462-76-6; (ketorolac trometamol) 74103-07-4; (loteprednol etabonate) 82034-46-6; (rimexolone) 49697-38-3; (chlorpheniramine) 132-22-9; (loratadine) 79794-75-5; (cetirizine) 83881-51-0, 83881-52-1; (terfenadine) 50679-08-8; (astemizole) 68844-77-9; (cyclosporin) 79217-60-0; (phenytoin) 57-41-0, 630-93-3; (fluorometholone) 426-13-1; (tetracycline) 23843-90-5, 60-54-8, 64-75-5; (doxycycline) 10592-13-9, 17086-28-1, 564-25-0

CHEMICAL NAME: Livostin; Emadine; Patanol; Acular; Alrex; Lotemax; Vexol; Claritin; Zyrtec; Flarex

L86 ANSWER 15 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1999138740 EMBASE
TITLE: Recent developments in ocular allergy.
AUTHOR: Nehmad L.
CORPORATE SOURCE: L. Nehmad, SUNY State College of Optometry, 100 East 24th Street, New York, NY 10010, United States
SOURCE: Clinical Eye and Vision Care, (1999) 11/1 (37-39).
Refs: 26
ISSN: 0953-4431 CODEN: CEVCEV
PUBLISHER IDENT.: S 0953-4431(99)00009-0
COUNTRY: Ireland
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 012 Ophthalmology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
***allergic conjunctivitis: ET, etiology**
***allergic conjunctivitis: DT, drug therapy**
*eye disease: ET, etiology
*eye disease: DT, drug therapy
***allergy: ET, etiology**
***allergy: DT, drug therapy**
disease classification
seasonal variation
vernal conjunctivitis
mast cell
eosinophil
short survey
Drug Descriptors:
*antihistaminic agent: DT, drug therapy
*stabilizing agent: DT, drug therapy
*nonsteroid antiinflammatory agent: DT, drug therapy

*corticosteroid: DT, drug therapy
levocabastine: DT, drug therapy
levocabastine: DV, drug development
nedocromil: DT, drug therapy
olopatadine: DT, drug therapy
olopatadine: DV, drug development
loteprednol etabonate: DT, drug therapy
loteprednol etabonate: DV, drug development
emedastine: DT, drug therapy
emedastine: DV, drug development
cyclosporin: DT, drug therapy
cell adhesion molecule: EC, endogenous compound
intercellular adhesion molecule 1: EC, endogenous compound
substance p: EC, endogenous compound
pentigetide: EC, endogenous compound
patenol
alrex
emadine

CAS REGISTRY NO.: (levocabastine) 79516-68-0; (nedocromil) 69049-73-6; (olopatadine) 113806-05-6, 140462-76-6; (loteprednol etabonate) 82034-46-6; (emedastine) 87233-61-2, 87233-62-3; (cyclosporin) 79217-60-0; (intercellular adhesion molecule 1) 126547-89-5; (substance p) 33507-63-0; (pentigetide) 62087-72-3

CHEMICAL NAME: Livostin; Patenol; Alrex; Emadine

L86 ANSWER 16 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999218575 EMBASE
TITLE: Allergies: New treatment options and studies.
AUTHOR: Evans Y.
CORPORATE SOURCE: Y. Evans, Univ. of Mississippi Hosp./Clinics, Jackson, MS, United States
SOURCE: Drug Topics, (7 Jun 1999) 143/11 SUPPL. (10s-15s).
ISSN: 0012-6616 CODEN: DGTNA7
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:

For years, antihistamines, decongestants, and corticosteroids have been the mainstay in treating allergic disorders. Today, the pharmacotherapy options are expanding, and more clinical trials are being conducted to determine the best treatments for the various allergic disorders. When chronic diseases, such as allergic disorders, affect one in five North Americans, it is important that pharmacists stay abreast of the treatment options that are available and under investigation.

CONTROLLED TERM: Medical Descriptors:
***allergy: DT, drug therapy**
***allergy: TH, therapy**
prophylaxis
drug safety
drug tolerability
cardiotoxicity: SI, side effect
anaphylaxis
clinical feature
drug efficacy
nose congestion

Searched by Barb O'Bryen, STIC 308-4291

immunotherapy
neurotoxicity: SI, side effect
gastrointestinal toxicity: SI, side effect
allergic rhinitis: DT, drug therapy
asthma: DT, drug therapy
allergic conjunctivitis: DT, drug therapy
eye disease
human
oral drug administration
intranasal drug administration
review
Drug Descriptors:
*antihistaminic agent: AE, adverse drug reaction
*antihistaminic agent: DT, drug therapy
*corticosteroid: DT, drug therapy
*decongestive agent: DT, drug therapy
*cholinergic receptor blocking agent: DT, drug therapy
*leukotriene receptor stimulating agent: DT, drug therapy
*histamine h1 receptor antagonist: AE, adverse drug reaction
*histamine h1 receptor antagonist: DT, drug therapy
terfenadine: AE, adverse drug reaction
terfenadine: DT, drug therapy
astemizole: AE, adverse drug reaction
astemizole: DT, drug therapy
cetirizine: DT, drug therapy
loratadine: CB, drug combination
loratadine: DT, drug therapy
fexofenadine: DT, drug therapy
azelastine: AE, adverse drug reaction
azelastine: CB, drug combination
azelastine: DT, drug therapy
montelukast: DT, drug therapy
zafirlukast: DT, drug therapy
zileuton: DT, drug therapy
loteprednol etabonate: AE, adverse drug reaction
loteprednol etabonate: DT, drug therapy
emedastine: AE, adverse drug reaction
emedastine: DT, drug therapy
ketotifen: AE, adverse drug reaction
ketotifen: DT, drug therapy
oxatomide: AE, adverse drug reaction
oxatomide: DT, drug therapy
ebastine: AE, adverse drug reaction
ebastine: DT, drug therapy
mizolastine: AE, adverse drug reaction
mizolastine: DT, drug therapy
tsukubaenolide: DT, drug therapy
fluticasone: CB, drug combination
fluticasone: DT, drug therapy
beclometasone: CB, drug combination
beclometasone: DT, drug therapy
cromoglycate disodium: DT, drug therapy
antazoline: CB, drug combination
antazoline: DT, drug therapy
antazoline: PR, pharmaceutics
naphazoline: CB, drug combination
naphazoline: DT, drug therapy
naphazoline: PR, pharmaceutics
glycerol: CB, drug combination
glycerol: DT, drug therapy
glycerol: PR, pharmaceutics
zinc sulfate: CB, drug combination

zinc sulfate: DT, drug therapy
zinc sulfate: PR, pharmaceutics
unindexed drug
alrex
emadine
fluticasone propionate

CAS REGISTRY NO.: (terfenadine) 50679-08-8; (astemizole) 68844-77-9; (cetirizine) 83881-51-0, 83881-52-1; (loratadine) 79794-75-5; (fexofenadine) 138452-21-8; (azelastine) 58581-89-8, 79307-93-0; (montelukast) 151767-02-1, 158966-92-8; (zafirlukast) 107753-78-6; (zileuton) 111406-87-2, 132880-11-6; (loteprednol etabonate) 82034-46-6; (emedastine) 87233-61-2, 87233-62-3; (ketotifen) 34580-13-7; (oxatomide) 60607-34-3; (ebastine) 90729-43-4; (mizolastine) 108612-45-9; (tsukubaenolide) 104987-11-3; (fluticasone) 90566-53-3; (beclometasone) 4419-39-0; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (antazoline) 154-68-7, 2508-72-7, 3131-32-6, 91-75-8; (naphazoline) 5144-52-5, 550-99-2, 835-31-4; (glycerol) 56-81-5; (zinc sulfate) 7733-02-0; (fluticasone propionate) 80474-14-2

CHEMICAL NAME: (1) Seldane; (2) Hismanal; (3) Zyrtec; (4) Claritin; (5) Allegra; (6) Astelin; (7) Singulair; (8) Zyflo; (9) Accolate; (10) Lotemax; (11) Alrex; (12) Emadine; (13) Zatiden; (14) Kestine; (15) Fk 506; (16) Cutivate

COMPANY NAME: (2) Janssen; (3) Pfizer; (4) Schering Plough; (5) Hoechst Marion Roussel; (6) Wallace; (7) Merck; (8) Abbott; (9) Zeneca; (11) Pharmos; (12) Alcon; (13) Novartis; (14) Rhone Poulenc Rorer; (15) Fujisawa; (16) Glaxo; Synthelabo

L86 ANSWER 17 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999062257 EMBASE
TITLE: Ocular allergic disease.
AUTHOR: Bhargava A.; Jackson W.B.; El-Defrawy S.R.
CORPORATE SOURCE: Dr. S.R. El-Defrawy, Department of Ophthalmology, University of Ottawa Eye Institute, 501 Smyth Road, Ottawa, Ont. K1H 8L6, Canada
SOURCE: Drugs of Today, (1998) 34/11 (957-971).
Refs: 39
ISSN: 0025-7656 CODEN: MDACAP
COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 012 Ophthalmology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Ocular allergy is a common condition that usually affects the conjunctiva of the eye and is therefore often referred to as allergic conjunctivitis. The severity of the disease can range from mild itching and redness, as seen in seasonal allergic conjunctivitis, to the more serious vision threatening forms of ocular allergy which affect the cornea, such as atopic keratoconjunctivitis. The pathogenesis of allergic conjunctivitis involves a complex mechanism which centers around IgE-mediated mast cell degranulation and release of multiple preformed and newly formed inflammatory mediators. The diagnosis of allergic conjunctivitis is usually a clinical one which can be made based on a thorough history and careful examination. Treatment of occular allergy should begin with conservative measures including allergen avoidance, environmental control, ocular irrigation and cold compresses. Pharmacotherapy of allergic conjunctivitis consists of several classes of drugs. Antihistamines are widely

used to treat mild conditions such as seasonal and perennial conjunctivitis and potent new agents such as levocabastine and emedastine are now available. Mast cell stabilizers such as sodium cromoglycate are both safe and effective and are commonly used in ocular allergy. More effective mast cell stabilizers such as nedocromil, lodoxamide and olopatadine are now being used. Nonsteroidal antiinflammatory drugs have demonstrated only limited efficacy and, as such, are not widely used. Topical steroids are very effective in treating signs and symptoms but are reserved for only refractory cases due to their serious side effects. Loteprednol and rimexelone are newer corticosteroids which reportedly have less of an effect on intraocular pressure. Cyclosporine has recently been shown to be highly effective in cases of vernal keratoconjunctivitis and atopic keratoconjunctivitis while producing no adverse effects.

CONTROLLED TERM: Medical Descriptors:
***allergic conjunctivitis: DI, diagnosis**
***allergic conjunctivitis: DT, drug therapy**
***allergic conjunctivitis: ET, etiology**
***allergic conjunctivitis: TH, therapy**
pathophysiology
clinical feature
antigen antibody reaction
eosinophil
drug induced disease: SI, side effect
sedation
eye irritation: SI, side effect
drug safety
drug efficacy
drug tolerability
drug potency
eye disease: SI, side effect
antiinflammatory activity
cataract: SI, side effect
human
controlled study
oral drug administration
topical drug administration
review
Drug Descriptors:
*antihistaminic agent: AE, adverse drug reaction
*antihistaminic agent: CB, drug combination
*antihistaminic agent: DT, drug therapy
*antibiotic agent: DT, drug therapy
*adrenergic receptor stimulating agent: CB, drug combination
*adrenergic receptor stimulating agent: DT, drug therapy
*nonsteroid antiinflammatory agent: AE, adverse drug reaction
*nonsteroid antiinflammatory agent: DT, drug therapy
*corticosteroid: AE, adverse drug reaction
*corticosteroid: DT, drug therapy
autacoid: EC, endogenous compound
astemizole: AE, adverse drug reaction
astemizole: DT, drug therapy
diphenhydramine: AE, adverse drug reaction
diphenhydramine: CB, drug combination
diphenhydramine: DT, drug therapy
loratadine: AE, adverse drug reaction
loratadine: DT, drug therapy
terfenadine: AE, adverse drug reaction
terfenadine: DT, drug therapy
pheniramine maleate: DT, drug therapy
mepyramine maleate: DT, drug therapy
antazoline: DT, drug therapy

levocabastine: AE, adverse drug reaction
levocabastine: DT, drug therapy
emedastine: DT, drug therapy
olopatadine: DT, drug therapy
cromoglycate disodium: AE, adverse drug reaction
cromoglycate disodium: DT, drug therapy
nedocromil: AE, adverse drug reaction
nedocromil: DT, drug therapy
pentigetide: AE, adverse drug reaction
pentigetide: DT, drug therapy
lodoxamide: AE, adverse drug reaction
lodoxamide: DT, drug therapy
ketorolac trometamol: DT, drug therapy
loteprednol etabonate: DT, drug therapy
rimexolone: DT, drug therapy
cyclosporin: AE, adverse drug reaction
cyclosporin: DT, drug therapy

CAS REGISTRY NO.: (astemizole) 68844-77-9; (diphenhydramine) 147-24-0, 58-73-1; (loratadine) 79794-75-5; (terfenadine) 50679-08-8; (pheniramine maleate) 132-20-7; (mepyramine maleate) 59-33-6; (antazoline) 154-68-7, 2508-72-7, 3131-32-6, 91-75-8; (levocabastine) 79516-68-0; (emedastine) 87233-61-2, 87233-62-3; (olopatadine) 113806-05-6, 140462-76-6; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (nedocromil) 69049-73-6; (pentigetide) 62087-72-3; (lodoxamide) 53882-12-5; (ketorolac trometamol) 74103-07-4; (loteprednol etabonate) 82034-46-6; (rimexolone) 49697-38-3; (cyclosporin) 79217-60-0

L86 ANSWER 18 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998344978 EMBASE
TITLE: The current and future therapy of allergic conjunctivitis.
AUTHOR: Friedlaender M.H.
CORPORATE SOURCE: Dr. M.H. Friedlaender, Division of Ophthalmology, MS214, Scripps Clinic, 10666 North Torrey Pines Road, La Jolla, CA 92037, United States
SOURCE: Current Opinion in Ophthalmology, (1998) 9/4 (54-58).
Refs: 14
ISSN: 1040-8738 CODEN: COOTEF
COUNTRY: United States
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
A wealth of antiallergic drugs is available for ocular allergy, and many new drugs will soon be approved. Pharmaceutical companies frequently seek approval of anti-inflammatory drugs for allergic indications, because it is relatively easy to perform clinical trials for ocular allergy. Extremely safe drugs for mild to moderate degrees of allergic conjunctivitis include antihistamines, mast cell stabilizers, and nonsteroidal anti-inflammatory agents. Topical corticosteroids, preferably those with reduced side effects, are available for more severe forms of ocular allergy. The choice of an antiallergic drug may be guided by the indication for which the drug was approved. The ultimate selection will be made based on the patient's symptoms, the drug's availability, and its cost.

CONTROLLED TERM: Medical Descriptors:
***allergic conjunctivitis: DT, drug therapy**
human
short survey

Searched by Barb O'Bryen, STIC 308-4291

priority journal
Drug Descriptors:
*olopatadine: DT, drug therapy
*pemirolast: DT, drug therapy
*nedocromil: DT, drug therapy
antiinflammatory agent: DT, drug therapy
antiallergic agent: DT, drug therapy
vasoconstrictor agent: DT, drug therapy
nonsteroid antiinflammatory agent: DT, drug therapy
levocabastine: DT, drug therapy
emedastine: DT, drug therapy
azelastine: DT, drug therapy
cromoglycate disodium: DT, drug therapy
lodoxamide trometamol: DT, drug therapy
prostaglandin synthase inhibitor: DT, drug therapy
corticosteroid: DT, drug therapy
fluorometholone: DT, drug therapy
rimexolone: DT, drug therapy
loteprednol etabonate: DT, drug therapy
cyclosporin: DT, drug therapy
3 isopropoxy 5 methoxy n (1h tetrazol 5 yl)benzo[b]thiophene 2 carboxamide: DT, drug therapy
pentigetide: DT, drug therapy
phosphodiesterase inhibitor: DT, drug therapy
CAS REGISTRY NO.: (olopatadine) 113806-05-6, 140462-76-6; (pemirolast) 69372-19-6; (nedocromil) 69049-73-6; (levocabastine) 79516-68-0; (emedastine) 87233-61-2, 87233-62-3; (azelastine) 58581-89-8, 79307-93-0; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (lodoxamide trometamol) 63610-09-3; (fluorometholone) 426-13-1; (rimexolone) 49697-38-3; (loteprednol etabonate) 82034-46-6; (cyclosporin) 79217-60-0; (3 isopropoxy 5 methoxy n (1h tetrazol 5 yl)benzo[b]thiophene 2 carboxamide) 104795-68-8; (pentigetide) 62087-72-3
CHEMICAL NAME: Ci 959

L86 ANSWER 19 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96370846 EMBASE
DOCUMENT NUMBER: 1996370846
TITLE: New directions in therapy for ocular allergy.
AUTHOR: El-Defrawy S.; Jackson W.B.
CORPORATE SOURCE: University of Ottawa Eye Institute, Ottawa General Hospital, 501 Smyth Road,Ottawa, Ont. K1H 8L6, Canada
SOURCE: International Ophthalmology Clinics, (1996) 36/2 (25-44). ISSN: 0020-8167 CODEN: IOPCAV
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 012 Ophthalmology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
***allergy: DI, diagnosis**
*eye disease: DT, drug therapy
drowsiness: SI, side effect
drug efficacy
drug mechanism
human
mast cell degranulation
oral drug administration
priority journal

review
topical drug administration
drug delivery system
Drug Descriptors:
*antihistaminic agent: CB, drug combination
*antihistaminic agent: DT, drug therapy
*antihistaminic agent: PD, pharmacology
*antihistaminic agent: AE, adverse drug reaction
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: PD, pharmacology
antazoline: CB, drug combination
antazoline: PD, pharmacology
antazoline: DT, drug therapy
astemizole: DT, drug therapy
astemizole: PD, pharmacology
chlorpheniramine: PD, pharmacology
chlorpheniramine: DT, drug therapy
chlorpheniramine: AE, adverse drug reaction
chlorpheniramine maleate
clemastine: DT, drug therapy
clemastine: AE, adverse drug reaction
clemastine: PD, pharmacology
clemastine fumarate
cromoglycate disodium: PD, pharmacology
cromoglycate disodium: DT, drug therapy
cyclosporin: DT, drug therapy
cyclosporin: PD, pharmacology
dexamethasone: PD, pharmacology
dexamethasone: DT, drug therapy
emedastine: DT, drug therapy
emedastine: PD, pharmacology
fluorometholone: PD, pharmacology
fluorometholone: DT, drug therapy
ketorolac: DT, drug therapy
ketorolac: PD, pharmacology
levocabastine: PD, pharmacology
levocabastine: DT, drug therapy
lodoxamide: PD, pharmacology
lodoxamide trometamol
loratadine: DT, drug therapy
loratadine: PD, pharmacology
loteprednol etabonate: DT, drug therapy
loteprednol etabonate: PD, pharmacology
naphazoline: CB, drug combination
naphazoline: DT, drug therapy
naphazoline: PD, pharmacology
nedocromil: PD, pharmacology
nedocromil: DT, drug therapy
pentapeptide: DT, drug therapy
pheniramine: CB, drug combination
pheniramine: PD, pharmacology
pheniramine: DT, drug therapy
prednisolone: PD, pharmacology
prednisolone: DT, drug therapy
rimexolone: PD, pharmacology
rimexolone: DT, drug therapy
suprofen: DT, drug therapy
suprofen: PD, pharmacology
terfenadine

CAS REGISTRY NO.: (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (antazoline) 154-68-7, 2508-72-7, 3131-32-6, 91-75-8; (astemizole) 68844-77-9; (chlorpheniramine) 132-22-9; (chlorpheniramine maleate)

Searched by Barb O'Bryen, STIC 308-4291

113-92-8; (clemastine) 15686-51-8; (clemastine fumarate) 14976-57-9; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (cyclosporin) 79217-60-0; (dexamethasone) 50-02-2; (emedastine) 87233-61-2, 87233-62-3; (fluorometholone) 426-13-1; (ketorolac) 74103-06-3; (levocabastine) 79516-68-0; (lodoxamide) 53882-12-5; (lodoxamide trometamol) 63610-09-3; (loratadine) 79794-75-5; (loteprednol etabonate) 82034-46-6; (naphazoline) 5144-52-5, 550-99-2, 835-31-4; (nedocromil) 69049-73-6; (pheniramine) 86-21-5; (prednisolone) 50-24-8; (rimexolone) 49697-38-3; (suprofen) 40828-46-4; (terfenadine) 50679-08-8

CHEMICAL NAME: Chlortrimeton; Tavist; Seldane; Hismanal; Claritin; Livostin; Alomide

```
=> fil medl; d que l13
FILE 'MEDLINE' ENTERED AT 12:59:45 ON 26 JUN 2003

 FILE LAST UPDATED: 25 JUN 2003 (20030625/UP). FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L1            2 SEA FILE=REGISTRY ABB=ON  LOTEPREDNOL?/CN
L4           52 SEA FILE=MEDLINE ABB=ON  LOTEPREDNOL# OR LOTEMAX OR ALREX OR
                LENOXIN OR CDDD5604 OR CDDD 5604 OR HGP1 OR HGP 1 OR P5604 OR
                P 5604 OR L1
L8       588794 SEA FILE=MEDLINE ABB=ON  C8./CT = Respiratory Tract Disease
L9       168638 SEA FILE=MEDLINE ABB=ON  HYPERSENSITIVITY+NT/CT
L10       13603 SEA FILE=MEDLINE ABB=ON  RHINITIS+NT/CT
L11        1313 SEA FILE=MEDLINE ABB=ON  CONJUNCTIVITIS, ALLERGIC/CT
L13          13 SEA FILE=MEDLINE ABB=ON  L4 AND (L8 OR L9 OR L10 OR L11)


=> fil embase; d que l46

FILE 'EMBASE' ENTERED AT 12:59:46 ON 26 JUN 2003
COPYRIGHT (C) 2003 Elsevier Science B.V. All rights reserved.

 FILE COVERS 1974 TO 19 Jun 2003 (20030619/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L31          118 SEA FILE=EMBASE ABB=ON  LOTEPREDNOL ETABONATE/CT
L38          607 SEA FILE=EMBASE ABB=ON  RHINOCONJUNCTIVITIS/CT
L39         7418 SEA FILE=EMBASE ABB=ON  ALLERGIC RHINITIS/CT
L46            3 SEA FILE=EMBASE ABB=ON  (L38 OR L39) AND L31


=> s l46 not l45

L87            1 L46 NOT (L45) previously printed

=> fil capl; d que l58

FILE 'CAPLUS' ENTERED AT 12:59:47 ON 26 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
```

FILE COVERS 1907 - 26 Jun 2003 VOL 138 ISS 26
FILE LAST UPDATED: 25 Jun 2003 (20030625/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L1             2 SEA FILE=REGISTRY ABB=ON  LOTEPREDNOL?/CN
L49           63 SEA FILE=CAPLUS ABB=ON  L1
L54         5895 SEA FILE=CAPLUS ABB=ON  RESPIRATORY TRACT/CW (L)(DISEASE# OR
                 DISORDER#)
L55         2574 SEA FILE=CAPLUS ABB=ON  RHINITIS/OBI
L56           77 SEA FILE=CAPLUS ABB=ON  RHINOCONJUNCTIVITIS/OBI
L57        18906 SEA FILE=CAPLUS ABB=ON  ALLERGY/CT
L58            7 SEA FILE=CAPLUS ABB=ON  L49 AND (L54 OR L55 OR L56 OR L57)


=> s l58 not l53

L88            5 L58 NOT L53
```

previously printed

```
=> dup rem l13,l88,l87
FILE 'MEDLINE' ENTERED AT 13:00:05 ON 26 JUN 2003

FILE 'CAPLUS' ENTERED AT 13:00:05 ON 26 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 13:00:05 ON 26 JUN 2003
COPYRIGHT (C) 2003 Elsevier Science B.V. All rights reserved.
PROCESSING COMPLETED FOR L13
PROCESSING COMPLETED FOR L88
PROCESSING COMPLETED FOR L87
L89           17 DUP REM L13 L88 L87 (2 DUPLICATES REMOVED)
                 ANSWERS '1-13' FROM FILE MEDLINE
                 ANSWERS '14-17' FROM FILE CAPLUS

=> d ibib ab hitrn 1-17

L89  ANSWER 1 OF 17     MEDLINE                          DUPLICATE 2
ACCESSION NUMBER:    1999083225     MEDLINE
DOCUMENT NUMBER:     99083225   PubMed ID: 9867336
TITLE:               The conjunctival provocation test model of ocular allergy:
                     utility for assessment of an ocular corticosteroid,
                     loteprednol etabonate.
AUTHOR:              Abelson M; Howes J; George M
CORPORATE SOURCE:    Ophthalmic Research Associates, North Andover,
                     Massachusetts, USA.
SOURCE:              JOURNAL OF OCULAR PHARMACOLOGY AND THERAPEUTICS, (1998 Dec)
                     14 (6) 533-42.
                     Journal code: 9511091. ISSN: 1080-7683.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       (CLINICAL TRIAL)
                     Journal; Article; (JOURNAL ARTICLE)
                     (RANDOMIZED CONTROLLED TRIAL)
LANGUAGE:            English
```

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990204

AB Two studies were conducted using the conjunctival provocation test (CPT) model of ocular allergy. The objective of the first study was to evaluate the sensitivity of the CPT model to a topical corticosteroid. Selected was **loteprednol** etabonate 0.5%, previously found effective in the treatment of ocular allergy and inflammation. The study was a randomized double-masked, placebo-controlled, paired-comparison of **loteprednol** etabonate 0.5% (LE), b.i.d. or q.i.d. Sixty subjects who had a minimum pre-determined allergic response received LE in one eye and placebo in the fellow eye for 28 days from Day 7 to Day 35. Antigen challenges were carried out on Days 0, 7 (baseline), 21 and 35. The primary endpoints were interocular differences in itching and mean redness (the average of ciliary, conjunctival and episcleral vessel beds). LE (either b.i.d. or q.i.d.) was significantly more effective than placebo for reducing mean redness and itching. No clinical or statistically significant changes in intraocular pressure were observed. Based upon the results of Study 1, we used the CPT model to aid in the selection of a concentration of **loteprednol** etabonate for subsequent studies in environmental seasonal allergic conjunctivitis. This was a randomized double-masked, placebo-controlled, paired-comparison of **loteprednol** etabonate 0.1%, 0.2% and 0.3%, q.i.d. in 88 subjects. The dosing and testing regimen was similar to the first portion of the study. **Loteprednol** etabonate, 0.1%, 0.2% and 0.3%, was numerically superior to the placebo in reducing mean redness and itching. At the 20-minute post allergen challenge, the 0.1% concentration was significantly superior ($p < 0.05$) to the placebo on Visit 4 (2 and 4 hour challenge) in reducing the mean redness; however, LE was only numerically superior in relieving itching. The 0.2% concentration was significantly superior ($p < 0.05$) to the placebo in the reduction of mean redness and itching on Visit 3 (Day 21) and in reduction of mean redness on Visit 4 (4 hour challenge). The 0.3% concentration was significantly superior ($p < 0.05$) to the placebo in the reduction of mean redness on all visits, and statistically significant in the reduction of itching on Visit 4 (4 hour challenge). While there were some elevations of IOP with LE 0.2%, they were not clinically significant. In conclusion, the CPT model of ocular allergy is useful in the evaluation of corticosteroids. Furthermore, based upon a dose-response study in this model, 0.2% **loteprednol** etabonate was selected for further evaluation in environmental seasonal allergic conjunctivitis studies.

L89 ANSWER 2 OF 17 MEDLINE
ACCESSION NUMBER: 2002622480 MEDLINE
DOCUMENT NUMBER: 22267675 PubMed ID: 12380639
TITLE: Compared topical ocular olopatadine 0.1% (Patanol) and **loteprednol** etabonate 0.2% (**Alrex**) in an allergen challenge model.
COMMENT: Comment on: Clin Ther. 2002 Jun;24(6):918-29
AUTHOR: Novack Gary D
SOURCE: CLINICAL THERAPEUTICS, (2002 Sep) 24 (9) 1477-8; author reply 1478-80.
Journal code: 7706726. ISSN: 0149-2918.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20021017
Last Updated on STN: 20030212

Searched by Barb O'Bryen, STIC 308-4291

Entered Medline: 20030211

L89 ANSWER 3 OF 17 MEDLINE
ACCESSION NUMBER: 2003023979 MEDLINE
DOCUMENT NUMBER: 22418341 PubMed ID: 12529966
TITLE: Basic HGF-like peptides inhibit generation of liver metastases in murine and human tumor models.
AUTHOR: Fazekas K; Raso E; Zarandi M; Dudas J; Timar J
CORPORATE SOURCE: Department of Tumor Progression, National Institute of Oncology, Institute of Pathology and Experimental Cancer Research, Semmelweis University, Budapest, Hungary.
SOURCE: ANTICANCER RESEARCH, (2002 Sep-Oct) 22 (5) 2575-9. Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20030118
Last Updated on STN: 20030221
Entered Medline: 20030220

AB PURPOSE: We have postulated that the peptide domain(s) of the heparin-binding cytokine(s) might have biological activity, which theoretically could be exploited for modulation of the biological behavior of cancer cells. MATERIALS AND METHODS: We used HGF as a model heparin-binding cytokine and synthesized two HGF beta-chain domains, HHRGK (**HGP1**) and RYRNKH (HGP2), as well as four variants. As target cells, we used three cancer cell lines (HT25 human colonic, HT168-M1/9 human melanoma and 3LL-HH murine lung carcinoma) all characterized by strong liver metastatic potentials. The effects of peptides on cell proliferation, tumor growth and liver metastasis were evaluated. RESULTS: All the basic penta- or hexapeptides exhibited similar antiproliferative effects in vitro in a dose range of 100-1000 ng/ml. Meanwhile, none of the HGP peptides exhibited significant antitumoral effects on the primary spleen tumors in the form of systemic treatment. However, systemic treatment with **HGP1**, but not with HGP2, applied at the early phase of the dissemination process, showed an inhibitory effect on liver metastatization of all the tumor lines studied. Furthermore, one out of the four hexapeptides, BP4 (KRKRKR), had similar activity. CONCLUSION: Recent data on the antiangiogenic effects of these basic peptides partially explain the in vivo antimetastatic activity. We suggest the small basic penta-hexapeptides as a new class of biological response modifiers which can modulate the metastatic process.

L89 ANSWER 4 OF 17 MEDLINE
ACCESSION NUMBER: 2002371627 MEDLINE
DOCUMENT NUMBER: 22111538 PubMed ID: 12117082
TITLE: Comparison of the clinical efficacy and tolerability of olopatadine hydrochloride 0.1% ophthalmic solution and **loteprednol** etabonate 0.2% ophthalmic suspension in the conjunctival allergen challenge model.
COMMENT: Comment in: Clin Ther. 2002 Sep;24(9):1477-8; discussion 1478-80
AUTHOR: Berdy Gregg J; Stoppel Juan O; Epstein Arthur B
CORPORATE SOURCE: Department of Ophthalmology, Washington University School of Medicine, St. Louis, USA.
SOURCE: CLINICAL THERAPEUTICS, (2002 Jun) 24 (6) 918-29. Journal code: 7706726. ISSN: 0149-2918.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20020716
Last Updated on STN: 20021218
Entered Medline: 20021217

AB BACKGROUND: Olopatadine hydrochloride 0.1% ophthalmic solution and **loteprednol** etabonate 0.2% ophthalmic suspension are topical antiallergic agents indicated for treatment of the signs and symptoms of allergic conjunctivitis and seasonal allergic conjunctivitis (SAC), respectively. OBJECTIVE: The purpose of this study was to compare the efficacy and tolerability of olopatadine, **loteprednol**, and placebo in inhibiting the early-phase allergic reaction (within 30 minutes) after conjunctival allergen challenge (CAC). METHODS: This was a single-center, randomized, double-masked, parallel-controlled CAC study. It consisted of 3 visits, with CAC performed at visit 1, confirmation and randomization at visit 2, and evaluation of the treatments at visit 3. Subjects with a history of allergic conjunctivitis were randomized to receive olopatadine, **loteprednol**, or placebo in a 2:2:1 ratio. Because **loteprednol** requires a loading period to achieve maximum efficacy, subjects assigned to this treatment received **loteprednol** QID bilaterally for a 14-day period; the olopatadine and placebo groups received placebo QID bilaterally during this period. At the evaluation visit, subjects received 1 drop of the assigned treatment in each eye. Fifteen minutes later, they were challenged with allergen. Subjects evaluated itching at 3, 5, and 10 minutes after challenge using a standardized 5-point scale; the investigator evaluated redness at 10, 15, and 20 minutes after challenge. Intraocular pressure (IOP) was measured at baseline and after the 14-day loading period. Nonparametric analyses were performed on the change from visit 2 to visit 3 in mean itching and redness scores for each time point, and on the change in mean IOP from visit 1 to visit 3. RESULTS: Fifty subjects (86% white; 42% male, 58% female; age range, 21-71 years) were enrolled and completed the study (20 olopatadine, 20 **loteprednol**, 10 placebo). The allergens to which subjects reacted were ragweed pollen (40%), cat hair or dander (30%), grass pollen (24%), and tree pollen (6%). The difference in inhibition of itching and redness was clinically significant (> or =1 unit difference) and statistically significant ($P < 0.05$) in favor of olopatadine compared with **loteprednol** at all 3 time points. The **loteprednol** group had a statistically significant increase in IOP after 2 weeks of treatment ($P < 0.001$). CONCLUSION: In the population studied, olopatadine was more efficacious than **loteprednol** in reducing the acute signs and symptoms of SAC during the early phase of the ocular allergic reaction and appeared to be better tolerated.

L89 ANSWER 5 OF 17 MEDLINE
ACCESSION NUMBER: 2002345286 MEDLINE
DOCUMENT NUMBER: 22082798 PubMed ID: 12088267
TITLE: Asthma therapy in the new millennium.
AUTHOR: Pahl A; Szelenyi I
CORPORATE SOURCE: Department of Experimental and Clinical Pharmacology and Toxicology, Friedrich-Alexander-University of Erlangen, Germany.. pahl@pharmakologie.uni-erlangen.de
SOURCE: INFLAMMATION RESEARCH, (2002 Jun) 51 (6) 273-82. Ref: 153
Journal code: 9508160. ISSN: 1023-3830.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20020629
Last Updated on STN: 20021217

Entered Medline: 20021212

AB Bronchial asthma is one of the most common chronic diseases in modern society and yet, despite the availability of highly effective drugs, there is increasing evidence to suggest that its incidence is increasing. It is a general health problem in several industrialised countries and will remain one for the next decades. With regard to asthma pathogenesis, our understanding has increased tremendously over the last two decades. Therefore, the potential for specific targeted and constructed therapies has become evident. Monoclonal antibodies to IgE, soluble receptors or antibodies to certain cytokines such as IL-4 and IL-5 are being investigated as possible treatments for asthma. Besides the already known receptor antagonists, new compounds directed to novel receptor types (e.g. cytokine, adenosine, adhesion molecules, etc.) are now under development. New targets in the cytosol will come into focus. Preliminary studies of selective phosphodiesterase (PDE) inhibitors in asthmatic patients have been encouraging. It is also very likely that the use of glucocorticoids cannot be excluded from therapy. However, we should generate new glucocorticoids with less side-effects, probably by using the so-called retrometabolic drug design. The first representative of this new steroid class, **loteprednol** is already approved for the therapy of certain allergic disorders. Because asthma is a disease of many different gene polymorphisms, gene therapy seems to be of low success at present. Alternatively, antisense oligonucleotides could be used. Future developments may also include strategies targeting the remodeling of structural elements of the airways. Today's intensive search for new treatments should ensure a greater diversity of therapeutic possibilities for the management of asthma in the next millennium.

L89 ANSWER 6 OF 17 MEDLINE
ACCESSION NUMBER: 2002144041 MEDLINE
DOCUMENT NUMBER: 21867952 PubMed ID: 11878194
TITLE: Drug therapy in asthma bronchiale in the new millennium.
AUTHOR: Szelenyi I; Pahl A
CORPORATE SOURCE: ASTA Medica AG, Radebeul, Germany.
SOURCE: PHARMAZIE, (2002 Feb) 57 (2) 83-6. Ref: 35
Journal code: 9800766. ISSN: 0031-7144.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020307
Last Updated on STN: 20020403
Entered Medline: 20020327

AB Asthma bronchiale represents a major health issue in industrialized countries and will likely remain so for decades. The drug treatment of asthma demonstrates certain peculiarities: revolutionary new drug introductions happen almost each quarter century. With improved understanding of asthma pathogenesis and drug metabolism, the potential for specific targeted and constructed therapies has become evident. Monoclonal antibodies to IgE and certain cytokines such IL-4 and IL-5 are being investigated as possible treatments for asthma. Similarly, preliminary studies of selective phosphodiesterase inhibitors in asthmatic patients have been encouraging. Other potential therapies include for example inhibitors of cytokine synthesis, promoters of Th2-Th1 switch, adenosine receptor agonists or antagonists, etc.. A new way is represented by a modified retrometabolic drug design resulting in so-called soft drugs. The first representative of this new drug class is **loteprednol** etabote (LE), a non-fluorinated glucocorticoid approved for the allergic ophthalmological indications and now in clinical trial for the treatment of allergic airway diseases. Today's intensive

search for new treatments should ensure a greater diversity of therapeutic possibilities for the management of asthma in the new millennium.

L89 ANSWER 7 OF 17 MEDLINE
ACCESSION NUMBER: 1999136642 MEDLINE
DOCUMENT NUMBER: 99136642 PubMed ID: 9951491
TITLE: A randomized, double-masked, placebo-controlled parallel study of **loteprednol** etabonate 0.2% in patients with seasonal allergic conjunctivitis.
AUTHOR: Shulman D G; Lothringer L L; Rubin J M; Briggs R B; Howes J; Novack G D; Hart K
CORPORATE SOURCE: Pharmos Corp., Alachua, Florida, USA.
SOURCE: OPHTHALMOLOGY, (1999 Feb) 106 (2) 362-9.
Journal code: 7802443. ISSN: 0161-6420.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990301
Last Updated on STN: 19990301
Entered Medline: 19990212
AB OBJECTIVE: To evaluate the effects of **loteprednol** etabonate (LE) 0.2% in reducing the signs and symptoms of seasonal allergic conjunctivitis. DESIGN: Randomized, double-masked, placebo-controlled, parallel group multicenter study of 6 weeks duration. PARTICIPANTS: A total of 135 patients with signs and symptoms of seasonal allergic conjunctivitis participated. INTERVENTION: All patients received either LE 0.2% or placebo (vehicle) four times a day in both eyes for 42 days. MAIN OUTCOME MEASURES: Bulbar conjunctival injection (primary sign) and itching (primary symptom) over the first 2 weeks of treatment was measured. RESULTS: A reduction in severity was seen in both LE and placebo groups for bulbar conjunctival injection (1.5 vs. 1.0 units on a 0-3 scale) and itching (3.4 vs. 3.0 units on a 0-4 scale) over the first 2 weeks. The treatment effect by these measures was -0.5 and -0.4 units in favor of LE ($P < or = 0.008$). Resolution (i.e., the proportion of patients with signs or symptoms no longer present) at day 14 strongly favored LE-treated patients (36% and 15%; 58% and 38%, for injection and itching, respectively). Both treatments were well tolerated. One patient in each treatment group (1 of 67 and 1 of 68, respectively) had an elevation of intraocular pressure of 10 mmHg or greater during the 6 weeks of treatment. CONCLUSIONS: **Loteprednol** etabonate 0.2% was more effective than placebo in the treatment of seasonal allergic conjunctivitis. **Loteprednol** etabonate 0.2% had a safety profile comparable to placebo.

L89 ANSWER 8 OF 17 MEDLINE
ACCESSION NUMBER: 1998379407 MEDLINE
DOCUMENT NUMBER: 98379407 PubMed ID: 9713785
TITLE: Change in intraocular pressure during long-term use of **loteprednol** etabonate.
AUTHOR: Novack G D; Howes J; Crockett R S; Sherwood M B
CORPORATE SOURCE: PharmaLogic, San Rafael, CA 94903, USA.
SOURCE: JOURNAL OF GLAUCOMA, (1998 Aug) 7 (4) 266-9.
Journal code: 9300903. ISSN: 1057-0829.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811

ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981106

AB PURPOSE: **Loteprednol** etabonate is a novel site-active corticosteroid synthesized through structural modifications of prednisolone-related compounds so that it will undergo a predictable transformation to an inactive metabolite. In double-masked studies, **loteprednol** etabonate was effective in the treatment of giant papillary conjunctivitis, seasonal allergic conjunctivitis, postoperative inflammation, and uveitis. The objective of this analysis was to determine the incidence of clinically significant elevations in intraocular pressure (IOP) with long-term use of **loteprednol** etabonate. PATIENTS AND METHODS: All subjects (healthy volunteers or patients with inflammation or allergy) in all sponsored **loteprednol** etabonate studies in the United States were evaluated. A clinically significant elevation in IOP was defined as > or = 10 mmHg at any visit, and long-term use was defined as > or = 28 days. Of the 2,210 subjects, 1,648 were treated for 28 days or longer with **loteprednol** etabonate (0.2% or 0.5%), prednisolone acetate 1%, or vehicle. RESULTS: IOP elevation > or = 10 mmHg occurred in 1.7% (15/901) of patients taking long-term **loteprednol** etabonate, 0.5% (3/583) of those taking vehicle, and 6.7% (11/164) of those taking prednisolone acetate. Excluding patients who wore contact lenses, the incidence was 0.6% (4/624), 1.0% (3/304), and 6.7% (11/164) for **loteprednol** etabonate, vehicle, and prednisolone acetate, respectively. The incidence of IOP elevations with 0.2% **loteprednol** etabonate was 0.8% (1/133), similar to that for vehicle (0.7%, 1/135). CONCLUSION: The results of this analysis in a large population of subjects undergoing long-term therapy and of a previously published controlled, double-masked study in corticosteroid responders suggest that **loteprednol** etabonate has less propensity to cause clinically significant elevations in IOP than prednisolone acetate.

L89 ANSWER 9 OF 17 MEDLINE
ACCESSION NUMBER: 1998389062 MEDLINE
DOCUMENT NUMBER: 98389062 PubMed ID: 9723669
TITLE: A randomized, double-masked, placebo-controlled parallel study of 0.2% **loteprednol** etabonate in patients with seasonal allergic conjunctivitis.
AUTHOR: Dell S J; Lowry G M; Northcutt J A; Howes J; Novack G D; Hart K
CORPORATE SOURCE: Texan Eye Care, Austin, USA.
SOURCE: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1998 Aug) 102 (2) 251-5.
Journal code: 1275002. ISSN: 0091-6749.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19981008
Last Updated on STN: 19981008
Entered Medline: 19980925

AB BACKGROUND: **Loteprednol** etabonate is a site-active corticosteroid with efficacy and safety in treating ocular inflammation at the 0.5% concentration. Evidence from dose-response studies suggested that the 0.2% concentration might be effective in treating ocular allergy. OBJECTIVES: The objective of this study was to evaluate the effects of 0.2% **loteprednol** etabonate in reducing the signs and symptoms of seasonal allergic conjunctivitis. METHODS: This was a randomized,

double-masked, placebo-controlled, parallel-group multicenter study. Patients with signs and symptoms of environmental seasonal allergic conjunctivitis received either **loteprednol** etabonate or placebo bilaterally four times daily for 42 days. RESULTS: Enrolled were 133 patients (66 receiving **loteprednol** etahonate; 67 receiving placebo). A reduction in severity was seen in both **loteprednol** etabonate and placebo groups for bulbar conjunctival injection (1.3 vs 0.9 units on a 0 to 3 scale) and itching (3.5 vs 3.1 units on a 0 to 4 scale) over the first 2 weeks. The treatment effect was -0.5 and -0.6 units in favor of **loteprednol** etabonate ($P < .001$). Resolution (the proportion of patients with the sign or symptom no longer present) at visit 4 (day 14) strongly favored **loteprednol** etabonate-treated patients over placebo-treated patients (31% and 9%, and 54% and 38%, for injection and itching, respectively). Both treatments were well tolerated. No patients in either treatment group (0 for **loteprednol** etabonate and 0 for vehicle) had an elevation of intraocular pressure of 10 mm Hg or greater during the 6 weeks of treatment. CONCLUSIONS: Loteprenol etabonate (0.2%) was more effective than placebo in the treatment of seasonal allergic conjunctivitis. **Loteprednol** etabonate (0.2%) had a safety profile comparable to placebo during this 6-week trial.

L89 ANSWER 10 OF 17 MEDLINE
ACCESSION NUMBER: 1998195301 MEDLINE
DOCUMENT NUMBER: 98195301 PubMed ID: 9535623
TITLE: A controlled evaluation of the efficacy and safety of **loteprednol** etabonate in the prophylactic treatment of seasonal allergic conjunctivitis. **Loteprednol** Allergic Conjunctivitis Study Group.
AUTHOR: Dell S J; Shulman D G; Lowry G M; Howes J
CORPORATE SOURCE: Texan Eye Care and Clinicor, Austin, USA.
SOURCE: AMERICAN JOURNAL OF OPHTHALMOLOGY, (1997 Jun) 123 (6) 791-7.
Journal code: 0370500. ISSN: 0002-9394.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980416
Last Updated on STN: 19980416
Entered Medline: 19980407
AB PURPOSE: To evaluate the efficacy and safety of **loteprednol** etabonate 0.5% as prophylactic treatment for the ocular signs and symptoms of seasonal allergic conjunctivitis. METHODS: In this randomized, double-masked, placebo-controlled, parallel study, 293 adults with history of seasonal allergic conjunctivitis were treated with either **loteprednol** etabonate or vehicle (placebo) four times daily, beginning before the onset of the allergy season and continuing for 6 weeks. The primary efficacy measure was a primary composite score (sum of itching and bulbar conjunctival injection scores). Supportive efficacy measures were the investigator global assessment and a secondary composite score (sum of tearing, erythema, chemosis, and discomfort scores), all calculated during the 21-day peak pollen season. RESULTS: The proportion of patients who never developed moderate or severe signs and symptoms of allergy during the peak pollen season in the **loteprednol** etabonate treatment group was greater than that in the placebo group. For the primary composite score, this efficacy criterion was reached by 94% of patients (136/145) in the **loteprednol** etabonate group and 78% of patients (111/143) in the placebo group ($P = .001$). The magnitude of

effect was similar for the investigator global assessment (86% [118/138] vs 64% [87/137]; P < .001) and, although not statistically significant, the secondary composite score (77% [112/145] vs 68% [97/143]; P = .092). None of the **loteprednol** etabonate-treated patients had an intraocular pressure increase of 10 mm Hg or more, whereas two placebo patients did. CONCLUSIONS: **Loteprednol** etabonate is generally effective in prophylaxis of seasonal allergic conjunctivitis and has an acceptable safety profile.

L89 ANSWER 11 OF 17 MEDLINE
ACCESSION NUMBER: 97255145 MEDLINE
DOCUMENT NUMBER: 97255145 PubMed ID: 9124242
TITLE: A double-masked, placebo-controlled evaluation of the efficacy and safety of **loteprednol** etabonate in the treatment of giant papillary conjunctivitis. The **Loteprednol** Etabonate Giant Papillary Conjunctivitis Study Group I.
AUTHOR: Friedlaender M H; Howes J
CORPORATE SOURCE: Scripps Clinic Medical Group, Inc, La Jolla, California 92037, USA.. mfried@scripps.edu
SOURCE: AMERICAN JOURNAL OF OPHTHALMOLOGY, (1997 Apr) 123 (4) 455-64.
Journal code: 0370500. ISSN: 0002-9394.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970506
Last Updated on STN: 19970506
Entered Medline: 19970423

AB PURPOSE: To evaluate the safety and effectiveness of **loteprednol** etabonate 0.5% ophthalmic suspension in reducing the ocular signs and symptoms accompanying contact lens-associated giant papillary conjunctivitis. METHODS: In a randomized, double-masked, placebo-controlled, parallel-group study conducted at 14 academic or private practice clinics, 223 adults with contact lens-associated giant papillary conjunctivitis received either **loteprednol** or the **loteprednol** vehicle (placebo), one drop, four times daily for 6 weeks. Papillae, itching, contact lens intolerance, other signs and symptoms of giant papillary conjunctivitis (0-to-3 or 0-to-4 grade scales), and intraocular pressure were measured. RESULTS: The proportion of patients treated with **loteprednol** who at final visit demonstrated an improvement in papillae of at least one grade (78%, 85/109) was significantly greater than the proportion of those treated with placebo (51%, 56/110; P = .001). A treatment difference favoring **loteprednol** was seen with improvement in itching (95% vs 81%, 104/109 vs 89/110; P < .001) and lens intolerance (87% vs 77%, 95/109 vs 85/110; P = .053). Eight of 109 patients (7%, all taking **loteprednol**) had an intraocular pressure increase of 10 mm Hg or more on at least one visit during treatment. After discontinuation of **loteprednol**, intraocular pressure returned to normal levels. Both treatments were well tolerated, and no serious unexpected treatment-related medical events were reported. CONCLUSIONS: The rapid therapeutic response combined with the low incidence and transient nature of any intraocular pressure increase suggests that **loteprednol** is an appropriate treatment for giant papillary conjunctivitis.

L89 ANSWER 12 OF 17 MEDLINE
ACCESSION NUMBER: 97155054 MEDLINE

DOCUMENT NUMBER: 97155054 PubMed ID: 9001768
TITLE: A double-masked, placebo-controlled evaluation of the efficacy and safety of **loteprednol** etabonate in the treatment of giant papillary conjunctivitis.
AUTHOR: Asbell P; Howes J
CORPORATE SOURCE: Mount Sinai Medical School, New York, NY 10029, USA.
SOURCE: CLAO JOURNAL, (1997 Jan) 23 (1) 31-6.
Journal code: 8302065. ISSN: 0733-8902.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970327
Last Updated on STN: 19970327
Entered Medline: 19970320

AB PURPOSE: To evaluate the safety and effectiveness of **loteprednol** etabonate 0.5% ophthalmic suspension (LE) for reducing the ocular signs and symptoms accompanying contact lens associated giant papillary conjunctivitis (GPC). We conducted a randomized, double-masked, placebo-controlled, parallel study at 11 U.S. academic or private practice clinics. METHODS: Two hundred and twenty adults with contact lens associated GPC were enrolled in this study. Patient were treated with either LE or the **loteprednol** etabonate vehicle (placebo), q.i.d. for 6 weeks. Papillae, itching, lens intolerance, as well as other signs and symptoms of GPC (0 to 3 or 0 to 4 point severity scales), and intraocular pressure were measured. RESULTS: The proportion of patients treated with LE demonstrating an improvement in papillae of at least one grade (75%) was significantly greater than the proportion of those treated with placebo (50%, $P < 0.001$). A treatment difference favoring LE was also seen with improvement in itching (92% vs. 76%, $P = 0.001$) and lens intolerance (84% vs. 66%, $P = 0.002$). Three patients (all on LE) had an intraocular pressure (IOP) elevation of 10 mm Hg or higher from baseline on at least one on-treatment visit. Cessation of therapy was required in one of these patients. CONCLUSIONS: Both treatments were well tolerated and no serious, unexpected, treatment-related medical events were reported. The rapid therapeutic response, combined with the low incidence, late development, and transient nature of any IOP elevation suggests that LE may be helpful in treating GPC.

L89 ANSWER 13 OF 17 MEDLINE
ACCESSION NUMBER: 93306984 MEDLINE
DOCUMENT NUMBER: 93306984 PubMed ID: 8319490
TITLE: Safety and efficacy of **loteprednol** etabonate for treatment of papillae in contact lens-associated giant papillary conjunctivitis.
AUTHOR: Bartlett J D; Howes J F; Ghormley N R; Amos J F; Laibovitz R; Horwitz B
CORPORATE SOURCE: Department of Optometry, School of Optometry, University of Alabama, Birmingham.
SOURCE: CURRENT EYE RESEARCH, (1993 Apr) 12 (4) 313-21.
Journal code: 8104312. ISSN: 0271-3683.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199308

Searched by Barb O'Bryen, STIC 308-4291

ENTRY DATE: Entered STN: 19930813
Last Updated on STN: 19930813
Entered Medline: 19930803

AB **Loteprednol** etabonate (LE) is a new corticosteroid based on the "soft drug" concept. Contact lens-associated giant papillary conjunctivitis (GPC) was studied as a model for the anti-inflammatory effect of LE. Patients with bilateral GPC were enrolled in a multicenter, randomized, double-masked, placebo-controlled, parallel group comparison of **loteprednol** etabonate 0.5% ophthalmic suspension and the LE vehicle (placebo). Patients were instructed to instill 1 drop of the test medication into each eye 4 times daily for 4 weeks, and follow-up examinations occurred on Days 2 or 3, 7, 14, 21, and 28 of masked therapy. Of 113 patients enrolled, 110 patients (LE = 55; placebo = 55) completed the study as planned. Patients receiving LE demonstrated significant reduction in the primary ocular signs of GPC (papillae, $p < 0.001$) and were rated better in the Investigator's Global Assessment ($p = 0.017$). LE did not elevate intraocular pressure during the study, and ratings for bulbar conjunctival injection and the Patient Opinion Assessment demonstrated statistical trends that favored treatment with LE. LE was well tolerated and was clinically effective for the treatment of GPC.

L89 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 2000:414694 CAPLUS
DOCUMENT NUMBER: 133:261550
TITLE: Loteprednol etabonate: a soft steroid for the treatment of allergic diseases of the airways
AUTHOR(S): Szelenyi, Istvan; Hochhaus, Gunther; Heer, Sabine; Kusters, Sabine; Marx, Degenhard; Poppe, Hildegard; Engel, Jurgen
CORPORATE SOURCE: Pulmonary Pharmacology, Corporate Research & Development, ASTA Medica, Frankfurt and Dresden, Germany
SOURCE: Drugs of Today (2000), 36(5), 313-320
CODEN: MDACAP; ISSN: 0025-7656
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 58 refs. There are several approaches for developing new antiallergic/antiasthmatic agents. One of them is the improvement of an existing class of effective drug classes. Due to some undesired effects of intranasal or inhaled corticosteroids, there is a need for better tolerated corticosteroids. Loteprednol etabonate belongs to the so-called class of soft steroids because it is metabolized by a 1-step reaction (hydrolysis) without using the cytochrome P 450 monooxygenase system. In in vitro investigations in human cells, loteprednol inhibited the release of proinflammatory cytokines (e.g., TNF-.alpha., GM-CSF, IL-4, IL-5) to an extent according to its relative binding potency to the glucocorticoid receptor. In in vivo animal studies, loteprednol effectively inhibited allergically induced vascular leakage in the nasal cavity of actively sensitized Brown Norway rats and rhinorrhea in actively sensitized domestic pigs following nasal challenge. In several models of allergic asthma, loteprednol was able to suppress the allergically induced late-phase eosinophilia in mice, rats and guinea pigs. After intrapulmonary administration of loteprednol, only a slight, nonsignificant redn. in thymus wt. was obsd. in a dose range far less than the therapeutically relevant doses. Its therapeutic ratio is clearly superior to those of beclomethasone and budesonide. Loteprednol is a safe steroid with an extremely wide range between therapeutic and side-effect-inducing doses. Its elimination profile, its pronounced binding to plasma protein and erythrocytes and its low oral bioavailability makes this drug highly suitable for nasal or pulmonary use.

IT **82034-46-6**, Loteprednol etabonate

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(loteprednol etabonate treatment of allergic diseases of the airways)
REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:832575 CAPLUS
DOCUMENT NUMBER: 137:346196
TITLE: Treatment of respiratory and lung diseases with antisense oligonucleotides and a bronchodilating agent
INVENTOR(S): Nyce, Jonathan W.; Li, Yukui; Sandrasagra, Anthony; Katz, Evan; Pabalan, Jonathan; Aguilar, Douglas; Miller, Shoreh; Tang, Lei; Shahabuddin, Syed
PATENT ASSIGNEE(S): Epigenesis Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 872 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085308	A2	20021031	WO 2002-US13135	20020423
WO 2002085308	A3	20021219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002085308	A2	20021031	WO 2002-XA13135	20020423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002085308	A2	20021031	WO 2002-XB13135	20020423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2002085308	A2	20021031	WO 2002-XC13135	20020423
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-286137P P 20010424
WO 2002-US13135 A 20020423

OTHER SOURCE(S): MARPAT 137:346196

AB This patent relates to a compn. comprising a carrier, oligonucleotides (oligos) that are antisense to adenosine receptors, and contain low amts. of or no adenosine (A), plus bronchodilating agents. All antisense oligonucleotides designed in accordance with the invention were highly effective at countering or reducing effects mediated by the receptors to which they are targeted. Two antisense phosphorothioated oligos targeting human adenosine A1 receptor mRNA, one targeting adenosine A2b receptor, and two targeting an A3 receptor are capable of countering the effect of exogenously administered adenosine which is mediated by the specific receptor they are targeted to. The activity of the antisense oligos are specific to the target and substitutively fail to inhibit another target. An oligonucleotide wherein the phosphodiester bonds are substituted with phosphorothioate bonds evidenced an unexpected superiority over the phosphodiester antisense oligo. In addn., they result in extremely low or non-existent deleterious side effects or toxicity. This represents 100% success in providing agents that are highly effective and specific in the treatment of bronchoconstriction and/or inflammation. Treatment with antisense oligonucleotides in combination with anti-inflammatory steroid and/or ubiquinones is also provided. These agents and the compn. and formulations provided are suitable for the treatment of respiratory tract, pulmonary and malignant diseases assocd. with bronchoconstriction, respiratory tract inflammation and allergies, impaired airways, including lung disease and diseases whose secondary effects afflict the lungs of a subject, such as allergies, asthma, impeded respiration, allergic rhinitis, pain, cystic fibrosis, pulmonary fibrosis, RDA, COPD, and cancers, among others. The present agents and compn. may be administered preventatively, prophylactically or therapeutically in conjunction with other therapies, or may be utilized as a substitute for therapies that have significant, neg. side effects. The method of the present invention is also practiced with antisense oligonucleotides targeted to many genes, mRNAs and their corresponding proteins in essential the same manner.

L89 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:385539 CAPLUS
DOCUMENT NUMBER: 137:346268
TITLE: Design and development of a soft corticosteroid, loteprednol etabonate
AUTHOR(S): Bodor, Nicholas; Buchwald, Peter
CORPORATE SOURCE: University of Florida, Gainesville, FL, USA
SOURCE: Lung Biology in Health and Disease (2002), 163(Inhaled Steroids in Asthma), 541-564
CODEN: LBHDD7; ISSN: 0362-3181
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Topical application of active corticosteroids that undergo nonoxidative, extrahepatic metab. can provide improved, safer treatments of allergic diseases by minimizing the risk of systemic absorption and, therefore, the occurrence of side effects. Loteprednol etabonate, a soft corticosteroid that contains 17.alpha.-carbonate and 17.beta. ester side chains and that was designed by using an inactive metabolite-based approach, lacks serious side effects and already received FDA approval for

use in all inflammatory and allergy-related ophthalmic disorders. Since exptl. evidence indicates that it also produces strong and long-lasting antiinflammatory effect after intranasal or intrapulmonary administration, currently it is being developed for the treatment of allergic conditions, such as rhinitis and asthma.

IT **82034-46-6**, Loteprednol etabonate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(design and development of soft corticosteroid loteprednol etabonate)

REFERENCE COUNT: 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:247172 CAPLUS
DOCUMENT NUMBER: 134:256899
TITLE: Combination of loteprednol and .beta.2-adrenoceptor agonists for the treatment of allergies and respiratory tract diseases
INVENTOR(S): Szelenyi, Istvan; Poppe, Hildegard; Heer, Sabine; Engel, Juergen
PATENT ASSIGNEE(S): Asta Medica Ag, Germany
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001022956	A2	20010405	WO 2000-EP9392	20000926
WO 2001022956	A3	20011011		
W: AU, BG, BR, BY, CA, CN, CZ, DZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19947235	A1	20010405	DE 1999-19947235	19990930
BR 2000014374	A	20020625	BR 2000-14374	20000926
EP 1216047	A2	20020626	EP 2000-969304	20000926
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003510276	T2	20030318	JP 2001-526168	20000926
EE 200200163	A	20030415	EE 2002-163	20000926

PRIORITY APPLN. INFO.: DE 1999-19947235 A 19990930
WO 2000-EP9392 W 20000926

AB The invention relates to a novel combination of a soft steroid, esp. loteprednol, and at least one .beta.2-adrenoceptor agonist for treating allergies and/or respiratory tract diseases simultaneously, sequentially or sep.; to drugs contg. said combination, to methods for producing such drugs and to the use of the novel combination for producing drugs for the simultaneous, sequential or sep. treatment of allergies and/or respiratory tract diseases. Thus and aerosol was prepd. that contained 6 .mu.g formoterol fumarate dihydrate and 200 .mu.g loteprednol per stroke. 2H-heptafluoropropane (1.000 g) propellant was cooled to -55.degree.C and 11.7 g Tagat TO in 11.7 g ethanol was added under stirring, followed by the addn. of 3.34 g micronized loteprednol etabonate and 0.1 g formoterol fumarate dihydrate. The suspension was dild. with 1,170.0 g 2H-heptafluoropropane, filled in metal containers with valves for dosing 50 .mu.L suspension per stroke.

IT **82034-46-6**, Loteprednol etabonate **129260-79-3**, Loteprednol

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(combination of loteprednol and .beta.2-adrenoceptor agonists for the treatment of allergies and respiratory tract diseases)

```
=> fil medl
FILE 'MEDLINE' ENTERED AT 13:01:21 ON 26 JUN 2003

 FILE LAST UPDATED: 25 JUN 2003 (20030625/UP).  FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que 128

L2            2 SEA FILE=REGISTRY ABB=ON  AZELASTINE/CN OR "AZELASTINE
                HYDROCHLORIDE"/CN
L5          444 SEA FILE=MEDLINE ABB=ON  AZELASTIN# OR A 5610 OR A5610 OR
                ASTELIN# OR OPTIVAR# OR ALLERGODIL# OR ASTELIN#
L6          352 SEA FILE=MEDLINE ABB=ON  AZEPTIN# OR "E0659" OR E 0659 OR
                W2979M OR W 2979M OR RHINOLAST# OR L2
L8       588794 SEA FILE=MEDLINE ABB=ON  C8./CT
L9       168638 SEA FILE=MEDLINE ABB=ON  HYPERSENSITIVITY+NT/CT
L10       13603 SEA FILE=MEDLINE ABB=ON  RHINITIS+NT/CT
L11        1313 SEA FILE=MEDLINE ABB=ON  CONJUNCTIVITIS, ALLERGIC/CT
L18         770 SEA FILE=MEDLINE ABB=ON  PHTHALAZINES/CT
L20         671 SEA FILE=MEDLINE ABB=ON  L18(L)(AD OR PD OR PK OR TU)/CT
L21         271 SEA FILE=MEDLINE ABB=ON  L20/MAJ AND (L5 OR L6)
L24      129176 SEA FILE=MEDLINE ABB=ON  (L8 OR L9 OR L10 OR L11)(L)(PC OR
                DT)/CT
L25       74032 SEA FILE=MEDLINE ABB=ON  L24/MAJ
L26         122 SEA FILE=MEDLINE ABB=ON  L21 AND L25
L27      944399 SEA FILE=MEDLINE ABB=ON  GENERAL REVIEW/DT
L28           7 SEA FILE=MEDLINE ABB=ON  L26 AND L27


=> s l28 not l13

L90           7 L28 NOT L13

=> fil embase

FILE 'EMBASE' ENTERED AT 13:01:24 ON 26 JUN 2003
COPYRIGHT (C) 2003 Elsevier Science B.V.  All rights reserved.

 FILE COVERS 1974 TO 19 Jun 2003 (20030619/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que 175

L32         1007 SEA FILE=EMBASE ABB=ON  AZELASTINE/CT
L35         1178 SEA FILE=EMBASE ABB=ON  ALLERGIC CONJUNCTIVITIS/CT
L36         1720 SEA FILE=EMBASE ABB=ON  ANTIALLERGIC AGENT/CT
L37       518140 SEA FILE=EMBASE ABB=ON  RESPIRATORY TRACT DISEASE+NT/CT
L38          607 SEA FILE=EMBASE ABB=ON  RHINOCONJUNCTIVITIS/CT
L39         7418 SEA FILE=EMBASE ABB=ON  ALLERGIC RHINITIS/CT
L40        23641 SEA FILE=EMBASE ABB=ON  ALLERGY/CT
```

previously printed

Subheadings
AD = administration & dosage
PD = pharmacology
PK = pharmacokinetics
TU = therapeutic use
PC = prevention & control
DT = drug therapy

```
L69      427343 SEA FILE=EMBASE ABB=ON  GENERAL REVIEW/DT
L71         823 SEA FILE=EMBASE ABB=ON  L32(L)(DT OR PK OR DO OR AD OR PD)/CT
L72         430 SEA FILE=EMBASE ABB=ON  L71/MAJ
L73       92022 SEA FILE=EMBASE ABB=ON  (L35 OR (L37 OR L38 OR L39 OR L40))(L)(
                DT OR PC)/CT
L74       74199 SEA FILE=EMBASE ABB=ON  L73/MAJ OR L36/MAJ
L75          20 SEA FILE=EMBASE ABB=ON  L72 AND L74 AND L69
```

Subheadings
DT = drug therapy
PK = pharmacokinetics
DO = dosage
AD = administration
PD = pharmacology
PC = prevention

=> s l75 not (145 or 187) previously printed

```
L91          20 L75 NOT (L45 OR L87)
```

=> fil capl; d que l67

```
FILE 'CAPLUS' ENTERED AT 13:01:26 ON 26 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 26 Jun 2003  VOL 138 ISS 26
FILE LAST UPDATED: 25 Jun 2003  (20030625/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

L2            2 SEA FILE=REGISTRY ABB=ON  AZELASTINE/CN OR "AZELASTINE
                HYDROCHLORIDE"/CN
L50         423 SEA FILE=CAPLUS ABB=ON  L2
L54        5895 SEA FILE=CAPLUS ABB=ON  RESPIRATORY TRACT/CW (L)(DISEASE# OR
                DISORDER#)
L55        2574 SEA FILE=CAPLUS ABB=ON  RHINITIS/OBI
L56          77 SEA FILE=CAPLUS ABB=ON  RHINOCONJUNCTIVITIS/OBI
L57       18906 SEA FILE=CAPLUS ABB=ON  ALLERGY/CT
L63         238 SEA FILE=CAPLUS ABB=ON  L50(L)(THU OR PAC OR BAC OR DMA OR
                PKT)/RL
L65     1643843 SEA FILE=CAPLUS ABB=ON  REVIEW/DT
L67           4 SEA FILE=CAPLUS ABB=ON  L63 AND (L54 OR L55 OR L56 OR L57) AND
                L65
```

=> s l67 not (188 or 153) previously printed

```
L92           4 L67 NOT (L88 OR L53)
```

=> dup rem l90,l92,l91
FILE 'MEDLINE' ENTERED AT 13:01:44 ON 26 JUN 2003

FILE 'CAPLUS' ENTERED AT 13:01:44 ON 26 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'EMBASE' ENTERED AT 13:01:44 ON 26 JUN 2003

PROCESSING COMPLETED FOR L90
PROCESSING COMPLETED FOR L92
PROCESSING COMPLETED FOR L91
L93 27 DUP REM L90 L92 L91 (4 DUPLICATES REMOVED)
ANSWERS '1-7' FROM FILE MEDLINE
ANSWERS '8-10' FROM FILE CAPLUS
ANSWERS '11-27' FROM FILE EMBASE

=> d ibib ab hitrn 1-27

L93 ANSWER 1 OF 27 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999169163 MEDLINE
DOCUMENT NUMBER: 99169163 PubMed ID: 10069901
TITLE: Management of allergic rhinitis with a combination antihistamine/anti-inflammatory agent.
AUTHOR: Lieberman P
CORPORATE SOURCE: Division of Allergy and Immunology and the Department of Pediatrics, University of Tennessee School of Medicine, Knoxville, USA.
SOURCE: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1999 Mar) 103 (3 Pt 2) S400-4. Ref: 39
Journal code: 1275002. ISSN: 0091-6749.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990413
AB **Azelastine** nasal spray is a topical antihistamine treatment for the symptoms of seasonal allergic rhinitis. Besides histamine antagonism, **azelastine** affects other chemical mediators of the inflammatory response including leukotrienes and kinins. This article reviews and discusses the antihistaminic and anti-inflammatory properties of **azelastine** and the results of pharmacokinetic studies and controlled clinical trials.

L93 ANSWER 2 OF 27 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1998328904 MEDLINE
DOCUMENT NUMBER: 98328904 PubMed ID: 9664202
TITLE: Intranasal **azelastine**. A review of its efficacy in the management of allergic rhinitis.
COMMENT: Erratum in: Drugs 1999 Jan;57(1):8
AUTHOR: McNeely W; Wiseman L R
CORPORATE SOURCE: Adis International Limited, Auckland, New Zealand.
SOURCE: DRUGS, (1998 Jul) 56 (1) 91-114. Ref: 1001
Journal code: 7600076. ISSN: 0012-6667.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19981008

Last Updated on STN: 20000303
Entered Medline: 19980928

AB **Azelastine**, a phthalazinone compound, is a second generation histamine H1 receptor antagonist which has shown clinical efficacy in relieving the symptoms of allergic rhinitis when administered as either an oral or intranasal formulation. It is thought to improve both the early and late phase symptoms of rhinitis through a combination of antihistaminic, antiallergic and anti-inflammatory mechanisms. Symptom improvements are evident as early as 30 minutes, after intranasal administration of **azelastine** [2 puffs per nostril (0.56mg)] and are apparent for up to 12 hours in patients with seasonal allergic rhinitis (SAR). The effect on nasal blockage is variable: in some studies objective and/or subjective assessment showed a reduction in blockage, whereas in other studies there was no improvement. Intranasal **azelastine** 1 puff per nostril twice daily is generally as effective as standard doses of other antihistamine agents including intranasal levocabastine and oral cetirizine, ebastine, loratadine and terfenadine at reducing the overall symptoms of rhinitis. The relative efficacies of **azelastine** and intranasal corticosteroids (beclomethasone and budesonide) remain unclear. However, overall, the corticosteroids tended to improve rhinitis symptoms to a greater extent than the antihistamine. **Azelastine** was well tolerated in clinical trials and postmarketing surveys. The most frequently reported adverse events were bitter taste, application site irritation and rhinitis. The incidence of sedation did not differ significantly between **azelastine** and placebo recipients and preliminary report showed cardiovascular parameters were not significantly altered in patients with perennial allergic rhinitis (PAR). Conclusion: Twice-daily intranasal **azelastine** offers an effective and well tolerated alternative to other antihistamine agents currently recommended for the symptomatic relief of mild to severe SAR and PAR in adults and children (aged > or = 12 years in the US; aged > or = 6 years in some European countries including the UK). The rapid onset, confined topical activity and reduced sedation demonstrated by the intranasal formulation of **azelastine** may offer an advantage over other antihistamine agents, although this has yet to be confirmed.

L93 ANSWER 3 OF 27 MEDLINE
ACCESSION NUMBER: 1999366455 MEDLINE
DOCUMENT NUMBER: 99366455 PubMed ID: 10437402
TITLE: [Second generation topical antihistaminics]. Leki przeciwhistaminowe drugiej generacji o dzialaniu miejscowym.
AUTHOR: Pietrzkowicz M; Grzelewska-Rzymowska I
CORPORATE SOURCE: Kliniki Pneumonologii i Alergologii IMW AM w Lodzi, Oddzial Ftizjopneumonologii.
SOURCE: POLSKI MERKURIUSZ LEKARSKI, (1999 May) 6 (35) 277-80. Ref: 59
Journal code: 9705469. ISSN: 1426-9686.
PUB. COUNTRY: Poland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Polish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990921
Last Updated on STN: 19990921
Entered Medline: 19990907

AB The article presents two topical antihistaminics: levocabastine and **azelastine**. Most attention is paid to discussing the pharmacokinetics and antihistamine, antiallergic and antiinflammatory activities of these drugs. Their clinical usefulness in allergic rhinitis

and conjunctivitis is also presented. Finally the authors describe the adverse reaction observed after administrating of topical antihistaminics.

L93 ANSWER 4 OF 27 MEDLINE
ACCESSION NUMBER: 1999407952 MEDLINE
DOCUMENT NUMBER: 99407952 PubMed ID: 10478514
TITLE: Efficacy and safety of **azelastine** nasal spray for the treatment of allergic rhinitis.
AUTHOR: Golden S J; Craig T J
CORPORATE SOURCE: PennState University College of Medicine, Hershey Medical Center, Hershey, Pa. 17033-0850, USA.
SOURCE: JOURNAL OF THE AMERICAN OSTEOPATHIC ASSOCIATION, (1999 Jul) 99 (7 Suppl) S7-12. Ref: 35
Journal code: 7503065. ISSN: 0098-6151.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19991012
Last Updated on STN: 19991012
Entered Medline: 19990930

AB **Azelastine** hydrochloride is a nasally administered antihistamine that is effective and safe for the treatment of perennial and seasonal allergic rhinitis. In addition to acting as a histamine H1-receptor antagonist, **azelastine** also inhibits the production or release of many chemical mediators of the allergic response such as leukotrienes, free radicals, and cytokines. After nasal administration, **azelastine** is systemically absorbed with a bioavailability of about 40%. The side effects of **azelastine** are drowsiness, headache, and bitter taste. **Azelastine** has a rapid onset of action with a benefit in about 2 hours and a prolonged duration of activity (12 to 24 hours). Studies have shown **azelastine** to be more effective than placebo in terms of reduction of the major and total symptom complexes of allergic rhinitis. Comparison studies have demonstrated that **azelastine** is as effective as ebastine, loratadine, cetirizine hydrochloride, and terfenadine at symptom reduction, with varying results when compared with the corticosteroids budesonide and beclomethasone. Although there are conflicting studies, some have demonstrated that **azelastine** reduces the nasal congestion of allergic rhinitis. This feature that distinguishes it from oral antihistamines is of great interest because corticosteroids are known to be quite effective for the relief of nasal congestion, whereas the antihistamines are effective for the sneezing, itchy eyes, itchy nose, and watery eyes, but not the congestion. **Azelastine** nasal spray seems to be an efficacious treatment for allergic rhinitis with a rapid onset and long duration of activity, but without the systemic adverse effects of traditional sedating antihistamines.

L93 ANSWER 5 OF 27 MEDLINE
ACCESSION NUMBER: 97108623 MEDLINE
DOCUMENT NUMBER: 97108623 PubMed ID: 8950949
TITLE: Inhibitor of chemical mediator release.
AUTHOR: Fujimura M
CORPORATE SOURCE: Third Department of Internal Medicine, Kanazawa University School of Medicine.
SOURCE: NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (1996 Nov) 54 (11) 3029-33. Ref: 8
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970305
Last Updated on STN: 19970305
Entered Medline: 19970219

AB Since tranilast, the first inhibitor of chemical mediator (ICMR), had been assessed to be as effective as disodium cromogycate in asthma, several orally active ICMRs, which have no antihistamine or bronchodilator effect, have been developed and prescribed for asthma control in Japan. On the other hand, as histamine H1-antagonists (H1-antagonists) have been shown to inhibit mediator release from mast cells in vitro, these drugs are sometimes classified as ICMR. ICMRs are effective in 40% of asthmatics but it takes 6 or more months for these drugs to improve the symptoms clearly. Although H1-antagonists are effective in only about 30% of asthmatics, they have been shown to be more effective on cough of asthma, cough variant asthma and atopic cough. H1-antagonists have been shown to strongly inhibit alcohol-induced asthma which is evoked in 60% of Japanese asthmatics.

L93 ANSWER 6 OF 27 MEDLINE
ACCESSION NUMBER: 93168241 MEDLINE
DOCUMENT NUMBER: 93168241 PubMed ID: 1363195
TITLE: Pharmacological treatment of allergies.
AUTHOR: De Vos C
CORPORATE SOURCE: UCB Pharma sector, Research and development, Braine-l'Alleud, Belgique.
SOURCE: ALLERGIE ET IMMUNOLOGIE, (1992 Dec) 24 (10) 382-4. Ref: 13
Journal code: 0245775. ISSN: 0397-9148.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199303
ENTRY DATE: Entered STN: 19930402
Last Updated on STN: 19950206
Entered Medline: 19930325

AB According to recent literature, the "anti-allergy" properties of antihistamines are linked to their antagonistic ability on receptor H1. In the majority of experimental models the immediate allergic responses is followed by a late phase. Especially at the pulmonary level, the presence of a late response after an allergic provocation is considered to correlate with the severity of asthma. The reference anti-allergy drugs, such as the inhaled corticosteroids or the cromones, without anti H1 activity, inhibit this late pulmonary response. **Azelastine**, ketotifen and cetirizine, three substances that are antagonistic to the anti-H1 receptor reduce the late pulmonary response. In addition, these three substances have other "anti-allergy" characteristics. **Azelastine** inhibits production of superoxide by the pulmonary neutrophils and eosinophils after PAF provocation in animals. Cetirizine significantly inhibits eosinophil infiltration in the bronchoalveolar lavage liquid in asthmatics with a late allergic bronchospasm. The presence of anti-histaminic and anti-allergy characteristics on the same molecule may perhaps convey a supplementary therapeutic benefit in the treatment of allergic symptoms.

L93 ANSWER 7 OF 27 MEDLINE
ACCESSION NUMBER: 92170637 MEDLINE
DOCUMENT NUMBER: 92170637 PubMed ID: 1686526

TITLE: **Azelastine**: a multifaceted drug for asthma therapy.
AUTHOR: Szelenyi I; Achterrath-Tuckermann U; Schmidt J; Minker E; Paegelow I; Werner H
CORPORATE SOURCE: Department of Pharmacology, ASTA Pharma AG, Frankfurt/Main, FRG.
SOURCE: AGENTS AND ACTIONS. SUPPLEMENTS, (1991) 34 295-311. Ref: 30
Journal code: 7801014. ISSN: 0379-0363.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 19920417
Last Updated on STN: 19950206
Entered Medline: 19920401

AB **Azelastine** (4-(p-chlorobenzyl)-2-(hexahydro-1-methyl-1H-azepin-4-yl)-1-(2H)-p hthalazinone hydrochloride), a novel long-acting antiasthmatic/antiallergic drug has been demonstrated to be effective in the treatment both of asthma and of allergic rhinitis. In this paper some selected properties of **azelastine** are presented which might contribute to its antiasthmatic and antiallergic effect. **Azelastine** causes a marked inhibition of generation of oxygen radicals in alveolar macrophages. A bronchosecretolytic activity of **azelastine** is observed which is based on the secretion of a more liquid mucus. Furthermore, the mucociliary clearance is enhanced as demonstrated in a rabbit model. Also IL-1 generation is inhibited in vitro and in vivo. Finally, the possible tissue and cellular accumulation of **azelastine** in lung and alveolar macrophages resp. is discussed.

L93 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 3
ACCESSION NUMBER: 1997:23772 CAPLUS
DOCUMENT NUMBER: 126:54329
TITLE: Local antihistamines
AUTHOR(S): Trigg, C. J.; Davies, R. J.
CORPORATE SOURCE: Department Allergy and Respiratory Medicine, Guy's Hospital, London, SE1 9RT, UK
SOURCE: Clinical and Experimental Allergy (1996), 26(10), 1108-1111
CODEN: CLEAEN; ISSN: 0954-7894
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 35 refs. Relief of acute symptoms is a priority in allergic rhinoconjunctivitis. This paper reviews H1 antihistamines as a highly effective treatment.

IT **58581-89-8**, Azelastine
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(local antihistamines for treatment of allergic **rhinoconjunctivitis** in humans)

L93 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:652253 CAPLUS
DOCUMENT NUMBER: 137:194885
TITLE: Clinical nasal decongestant activity with oral antihistamines
AUTHOR(S): Howarth, P.

Searched by Barb O'Bryen, STIC 308-4291

CORPORATE SOURCE: Southampton General Hospital, Southampton, UK
SOURCE: Clinical & Experimental Allergy Reviews (2002), 2(3), 101-106
CODEN: CEARC3; ISSN: 1472-9725
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Allergic rhinitis is an inflammatory condition with increasing prevalence in many developed countries. Although first-generation antihistamines have shown efficacy in the treatment of this disease, they are relatively ineffective for the treatment of nasal blockage. By contrast, studies with newer antihistamines, such as fexofenadine, ceitrizine, mizolastine, desloratadine, and azelastine, have shown efficacy in reducing all symptoms of allergic rhinitis, including nasal congestion. This paper focuses on the clin. studies that have been carried out with some of the newer antihistamines and discusses the mechanisms by which they may exert their addnl. anti-allergic effects.
IT **58581-89-8**, Azelastine
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(clin. nasal decongestant activity with oral antihistamines)
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L93 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:697059 CAPLUS
DOCUMENT NUMBER: 136:77
TITLE: Treatment update: Allergic **rhinitis**
AUTHOR(S): Berger, William E.
CORPORATE SOURCE: Mission Viejo Medical Center, Mission Viejo, CA, 92691, USA
SOURCE: Allergy and Asthma Proceedings (2001), 22(4), 191-198
CODEN: AAPRFV; ISSN: 1088-5412
PUBLISHER: OceanSide Publications, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. In addn. to the introduction of several new pharmacol. agents, two of the most significant recent developments in the management of allergic rhinitis have been the renewed emphasis on preventive measures, such as allergen avoidance and immunotherapy, and the importance of performing an accurate differential diagnosis of the disease. Recently, these evolving management trends were delineated in an algorithm proposed by the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunol., which suggests that an initial evaluation be performed by a primary care physician. Based on findings at the initial evaluation, the patient should be treated either empirically in the primary care setting or referred to an allergist-immunologist for consultation. The allergist uses an evidence-based therapeutic approach based on a differential diagnosis of the type of rhinitis, which uses information derived from a detailed medical history, phys. examn. of the airway, and ancillary tests, particularly skin tests. Rhinitis management by an allergist emphasizes a three-pronged approach that incorporates avoidance, immunotherapy, and pharmacol. therapy. However, because both avoidance and immunotherapy have their limitations, pharmacol. therapy remains the mainstay of rhinitis management, and allergists usually recommend that optimal first-line therapy be broad based and capable of safely alleviating the symptoms of both allergic and nonallergic disease. First generation oral antihistamines, topical corticosteroids and the topical antihistamine azelastine are the most broad-based treatments available. Second-generation oral antihistamines and leukotriene antagonists also are useful in treating allergic rhinitis.
IT **58581-89-8**, Azelastine
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(management of allergic **rhinitis** in humans)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L93 ANSWER 11 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001192825 EMBASE
TITLE: Update on nonallergic rhinitis.
AUTHOR: Settipane R.A.; Lieberman P.
CORPORATE SOURCE: Dr. R.A. Settipane, Brown University School of Medicine, 95 Pittman Street, Providence, RI 02906, United States. setti5@aol.com
SOURCE: Annals of Allergy, Asthma and Immunology, (2001) 86/5 (494-507).
Refs: 93
ISSN: 1081-1206 CODEN: ALAIF6
COUNTRY: United States
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 011 Otorhinolaryngology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: Although nonallergic rhinitis is a well recognized entity, its incidence and therapy have not been definitively studied. Recent epidemiologic studies and treatment trials have furthered our knowledge regarding the frequency of occurrence of this disorder and effective treatment modalities. Objective: To review and put into perspective recent advances in our knowledge regarding the incidence and significance as well as therapy of chronic nonallergic rhinitis. In addition, based upon these data, to propose a classification of this disorder. Data Sources: The MEDLINE database and the results of a national survey of allergists (National Rhinitis Task Force) conducted in 15 allergy practices involving 975 patients. Conclusions: Nonallergic rhinitis is a common disease that probably affects as many as 17 million Americans. Of equal importance is that, based on available data, approximately 22 million people suffer with a combination of nonallergic rhinitis and allergic diseases (mixed rhinitis). Both nonallergic and mixed rhinitis occur more frequently in adults than in children, may be more common in female patients than in male patients, and are more likely to be perennial than seasonal. Agents demonstrating efficacy (based on controlled trials or having approval by the FDA) for the therapy of nonallergic rhinitis are azelastine and topical nasal steroids.

L93 ANSWER 12 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000164377 EMBASE
TITLE: Interleukin 4 as a therapeutic target in allergic disorders.
AUTHOR: Snell N.J.C.
CORPORATE SOURCE: N.J.C. Snell, Bayer Pharma, Stoke Court, Stoke Poges SL2 4LY, United Kingdom. noel.snell.ns@bayer.co.uk
SOURCE: Current Opinion in Anti-inflammatory and Immunomodulatory Investigational Drugs, (2000) 2/2 (92-99).
Refs: 84
ISSN: 1464-8474 CODEN: COAIFF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
030 Pharmacology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Interleukin-4 (IL-4) is a cytokine which is considered to play a pivotal role in the pathogenesis of allergic disorders, and hence has been identified as a possible therapeutic target. Several agents have been shown to interfere with the expression, biosynthesis, secretion, or signal transduction of IL-4. Two novel approaches involve neutralization of circulating IL-4 by monoclonal antibodies, or by soluble IL-4 receptors; and blockade of the IL-4 receptor by mutant forms of IL-4. Both approaches show promise in vivo.

L93 ANSWER 13 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000040732 EMBASE
TITLE: Is the use of benzalkonium chloride as a preservative for nasal formulations a safety concern? A cautionary note based on compromised mucociliary transport.
AUTHOR: Bernstein I.L.
CORPORATE SOURCE: Dr. I.L. Bernstein, Univ. of Cincinnati College of Med., 231 Bethesda Ave, Cincinnati, OH 45267, United States
SOURCE: Journal of Allergy and Clinical Immunology, (2000) 105/1 I (39-44).
Refs: 30
ISSN: 0091-6749 CODEN: JACIBY
COUNTRY: United States
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: Topical nasal solution and suspension delivery systems are available for short- and long-acting vasoconstrictors, ipratropium, cromolyn, azelastine, and glucocorticosteroids. The use of intranasal glucocorticosteroids has increased substantially because the efficacy of these agents has been well established for the treatment of perennial and seasonal allergic rhinitis. Adverse local effects of burning, irritation, and dryness are occasionally associated with glucocorticosteroid nasal preparations. Benzalkonium chloride (BKC) is a quaternary ammonium antimicrobial agent included in some nasal solutions (including glucocorticosteroids) to prevent the growth of bacteria. Some reports suggest that BKC in nasal sprays may cause adverse effects, including reduced mucociliary transport, rhinitis medicamentosa, and neutrophil dysfunction. Objective: This article summarizes recent literature about possible adverse biologic effects associated with BKC as a nasal spray preservative by examining its effects on the following properties of mucociliary transport: ciliary motion, ciliary form, ciliary beat frequency, electron microscopy, and particle movement/saccharin clearance tests. Conclusion: Both animal and human in vitro data suggest that BKC promotes ciliostasis and reduction in mucociliary transport that may be partially masked by absorption and dilution effects occurring in respiratory mucus. These possible confounding factors may account for several disparate human in vivo results. The use of BKC-free glucocorticosteroid formulations should be considered, particularly in patients who complain of nasal burning, dryness, or irritation.

L93 ANSWER 14 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999303030 EMBASE
TITLE: [Histamine and leukotrienes in allergic rhinitis].
HISTAMIN UND LEUKOTRIENE BEI DER ALLERGISCHEN RHINITIS.
AUTHOR: Bachert C.; Lange B.
CORPORATE SOURCE: C. Bachert, Kliniek Neus-, Keel- en Oorheelkunde, UZ Gent, De Pintelaan 185, B-9000 Gent, Belgium
SOURCE: Allergologie, (1999) 22/8 (492-507).
Refs: 105

ISSN: 0344-5062 CODEN: ALLRDI
COUNTRY: Germany
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 011 Otorhinolaryngology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: English; German
AB Our knowledge about the pathophysiology of allergic rhinitis has been enriched in recent years by the investigation of different mediators (e.g. cytokines), involved cells like mast cells or eosinophils, and mechanisms like the adhesion cascade. This has led to the realization that allergic rhinitis is a persistent inflammation. While histamine is still considered the most important mediator of early phase reaction and mainly responsible for the symptoms sneezing, itching and rhinorrhea, other mediators like leukotrienes became matters of further scientific interest. Leukotrienes play an important role in nasal congestion, secretion and infiltration. Thus inhibition of leukotriene synthesis and action seems to be promising in the therapy of allergic rhinitis, especially regarding nasal congestion. Azelastine and mizolastine, two second generation histamine H1-antagonists possess anti-inflammatory leukotriene-antagonistic properties. Their efficacy in the treatment of nasal obstruction has been proven in various studies.

L93 ANSWER 15 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998277145 EMBASE
TITLE: Overview of diagnosis and management of allergic rhinitis.
AUTHOR: Urval K.R.
CORPORATE SOURCE: Dr. K.R. Urval, Ohio Valley Asthma and Allergy Inst., 2101 Jacob Street, Wheeling, WV 26003, United States
SOURCE: Primary Care - Clinics in Office Practice, (1998) 25/3 (649-662).
Refs: 14
ISSN: 0095-4543 CODEN: PRCADR
COUNTRY: United States
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 011 Otorhinolaryngology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Allergic rhinitis remains an important problem that affects people of all ages. Although allergic rhinitis is considered a trivial disease by the public and medical community alike, the evidence of allergic rhinitis as a risk factor to the development of associated diseases such as asthma, sinusitis, otitis media with effusion, and nasal polyps is better appreciated. Pathophysiology and current therapy of allergic rhinitis is reviewed.

L93 ANSWER 16 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998263886 EMBASE
TITLE: Differentiating and treating allergic rhinitis.
AUTHOR: Frieri M.
CORPORATE SOURCE: Dr. M. Frieri, Nassau County Medical Center, East Meadow, NY, United States
SOURCE: IM - Internal Medicine, (1998) 19/6 (44-48).
Refs: 16
ISSN: 1056-9286 CODEN: IMEIEI
COUNTRY: United States
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 011 Otorhinolaryngology

026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Allergic rhinitis doesn't just make people miserable; its complications can be quite serious. Review the keys to accurate diagnosis and effective management of this widespread disorder.

L93 ANSWER 17 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97289611 EMBASE
DOCUMENT NUMBER: 1997289611
TITLE: Updates of cabergoline and azelastine nasal spray.
AUTHOR: Levien T.; Baker D.E.
CORPORATE SOURCE: D.E. Baker, Drug Information Center, Professor of Pharmacy Practice, Washington State University, 601 West First Avenue, Spokane, WA 99204-0399, United States
SOURCE: Hospital Pharmacy, (1997) 32/9 (1252-1270).
Refs: 29
ISSN: 0018-5787 CODEN: HOPHAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 003 Endocrinology
011 Otorhinolaryngology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L93 ANSWER 18 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96271313 EMBASE
DOCUMENT NUMBER: 1996271313
TITLE: [Azelastin, a novel antiallergic agent]. AZELASTINA, UM NOVO AGENTE ANTIALERGICO.
AUTHOR: Korolkovas A.; Haraguchi T.
CORPORATE SOURCE: Departamento de Farmacia, Faculdade de Ciencias Farmaceuticas, Universidade de Sao Paulo,Sao Paulo, Brazil
SOURCE: Revista Brasileira de Medicina, (1996) 53/8 (786-796).
ISSN: 0034-7264 CODEN: RBMEAU
COUNTRY: Brazil
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 011 Otorhinolaryngology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: Portuguese
SUMMARY LANGUAGE: English; Portuguese
AB The pharmacologic actions, pharmacokinetic, adverse effects, therapeutic uses, dosage and administration, mechanism action and comparison with other antihistaminics H1 of azelastine are reviewed.

L93 ANSWER 19 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97187048 EMBASE
DOCUMENT NUMBER: 1997187048
TITLE: [Nasal hypersensitivity. Allergic rhinitis and its differential diagnosis. Consensus report on its pathophysiology, classification, diagnosis and treatment]. DIE NASALE HYPERREAKTIVITAT. DIE ALLERGISCHE RHINITIS UND IHRE DIFFERENTIALDIAGNOSEN. KONSENSUSBERICHT ZUR PATHOPHYSIOLOGIE, KLASSIFIKATION, DIAGNOSE UND THERAPIE.
AUTHOR: Bachert C.; Ganzer U.
CORPORATE SOURCE: C. Bachert, HNO-Klinik/Poliklinik, Heinrich-Heine-

Universitat, Moorenstrasse 5, D-40225 Dusseldorf, Germany
SOURCE: Oto-Rhino-Laryngologia Nova, (1996) 6/5-6 (287-300).
Refs: 57
ISSN: 1014-8221 CODEN: OTNOEQ
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 011 Otorhinolaryngology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: German

L93 ANSWER 20 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96332822 EMBASE
DOCUMENT NUMBER: 1996332822
TITLE: Antiallergic properties of antihistamines.
AUTHOR: Negro-Alvarez J.M.; Funes E.; Garcia Canovas A.; Hernandez J.; Garcia-Selles F.J.; Pagan J.A.; Lopez-Sanchez J.D.
CORPORATE SOURCE: Residencial 'La Paloma' A-1,30120 El Palmar, Murcia, Spain
SOURCE: Allergologia et Immunopathologia, (1996) 24/4 (177-183).
ISSN: 0301-0546 CODEN: AGIMBJ
COUNTRY: Spain
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English; Spanish
AB Histamine is a major mediator of the allergic reaction, and histamine H1-receptor antagonists have a long history of clinical efficacy in a variety of allergic disorders. The pathogenesis of allergic disease is complex, involving not only histamine and mast cell-derived tryptase, but also eosinophil and neutrophil derived mediators, cytokines, and intercellular adhesion molecules (ICAM-1). A number of 'in vitro' and 'in vivo' studies have been performed to assess the clinical effectiveness of antihistamines in inhibiting the allergen-induced inflammatory process in the skin and mucosa. In vitro human studies have shown that high concentration of second generation antihistamines can block inflammatory mediator release from basophils and mast cells, and reduce ICAM-1 expression in epithelial cell lines. In vivo studies have also shown an effect on the allergen-induced inflammatory reaction; both oral and intranasal antihistamines cause a reduction in nasal symptoms and inflammatory cell influx. Analysis of secretory fluids and tissues after challenge indicates that antihistamines interfere with mediator release. Recruitment of inflammatory cells to the site of the allergic insult is also disturbed by antihistamines of second-generation, suggesting that these drugs may inhibit upregulation of molecules involved in cell adhesion and migration, and perhaps they may interfere with the cytokine cascade through their ability of stabilizing mast cells and of limiting the incursion of inflammatory cells. This article reviews available human data on the antiallergic effects of antihistamines.

L93 ANSWER 21 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96030257 EMBASE
DOCUMENT NUMBER: 1996030257
TITLE: [Treatment of allergic rhinoconjunctivitis with antihistamines and non steroid anti-inflammatory medications].
RHINOCONJUNCTIVITE ALLERGIQUE: PLACE DES ANTIHISTAMINIQUES ET DES ANTI-INFLAMMATOIRES NON STEROIDIENS.
AUTHOR: Hammann C.; Spertini F.
CORPORATE SOURCE: Division d'Immunologie/Allergie, CHUV,1011 Lausanne, Switzerland
SOURCE: Medecine et Hygiene, (1996) 54/2099 (10-15).

ISSN: 0025-6749 CODEN: MEHGAB
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
011 Otorhinolaryngology
012 Ophthalmology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: French
SUMMARY LANGUAGE: French; English

AB Two antihistamines (levocabastine and azelastine) and an anti-inflammatory non steroidal agent (nedocromil sodium), have recently been developed for topical treatment of rhinoconjunctivitis. If in rhinitis, antihistamine H1-receptor improves rhinorrhea, pruritus and sneezing, topical steroids are still considered as the best treatment of nasal obstruction. Efficacy of antihistamines and nedocromil sodium has been demonstrated in multiple seasonal studies compared to placebo, and both medications constitute currently the basis of therapy for allergic conjunctivitis. Because of its good tolerance, in asthma as well as in conjunctivitis and rhinitis, and though its efficacy is inferior to that of topical steroids, the development of a medication such as nedocromil sodium arouses marked interest.

L93 ANSWER 22 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95175066 EMBASE
DOCUMENT NUMBER: 1995175066
TITLE: Azelastine a novel in vivo inhibitor of leukotriene biosynthesis: A possible mechanism of action: A mini review.
AUTHOR: Chand N.; Sofia R.D.
CORPORATE SOURCE: Wallace Laboratories, P.O. Box 1001,Cranbury, NJ 08512, United States
SOURCE: Journal of Asthma, (1995) 32/3 (227-234).
ISSN: 0277-0903 CODEN: JOUADU
COUNTRY: United States
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Leukotrienes have been proposed as important chemical mediators of allergic inflammation, and there is evidence that azelastine (Astelin.RTM.) can affect leukotriene-mediated allergic responses. One of the enzymes required for the synthesis of leukotrienes from arachidonic acid is 5-lipoxygenase (5-LO). Azelastine, which is preferentially taken up by the lung and alveolar macrophages, inhibits leukotriene generation in the airways. This property of azelastine may contribute to its therapeutic efficacy in the long-term treatment and management of rhinitis and asthma. Azelastine does not directly inhibit 5-LO in disrupted murine peritoneal cells and rat basophilic leukemia cells (IC50 > 100 .mu.M), but does have moderate 5-LO inhibitory activity in intact murine peritoneal cells (IC50 = 10 .mu.M, 5 min) and in chopped guinea pig liver (IC50 = 14 .mu.M, 2 hr). The generation and release of leukotrienes in human neutrophils and eosinophils is also inhibited by azelastine (IC50 = 0.9-1.1 .mu.M). Furthermore, azelastine is a potent and specific inhibitor of allergen-induced generation of leukotrienes in the nose of the guinea pig (ID50 < 100 .mu.g/kg, im, 20 min) as well as in patients with rhinitis (2 mg, po, 4 hr; ID50 < 30 .mu.g/kg). Azelastine also inhibits allergen-induced, leukotriene-mediated, pyrilamine-resistant bronchoconstriction (oral ID50 = 60 .mu.g/kg, 2 hr and 120 .mu.g/kg, 24 hr). This profile suggests that azelastine may be a novel inhibitor of 2

Ca2+-dependent translocation of 5-lipoxygenase from cytosol to the nuclear envelope or a FLAP inhibitor rather than a direct 5-LO inhibitor.

L93 ANSWER 23 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95146143 EMBASE
DOCUMENT NUMBER: 1995146143
TITLE: A comparison of the pharmacodynamics of H1-receptor antagonists as assessed by the induced wheal-and-flare model.
AUTHOR: Juhlin L.
CORPORATE SOURCE: Department of Dermatology, University Hospital,Uppsala, Sweden
SOURCE: Allergy: European Journal of Allergy and Clinical Immunology, Supplement, (1995) 50/24 (24-30).
ISSN: 0108-1675 CODEN: ALSUET
COUNTRY: Denmark
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 013 Dermatology and Venereology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L93 ANSWER 24 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92035394 EMBASE
DOCUMENT NUMBER: 1992035394
TITLE: Comparative efficacy of H1 antihistamines.
AUTHOR: Aaronson D.W.
CORPORATE SOURCE: 9301 Golf Road,Des Plaines, IL 60016, United States
SOURCE: Annals of Allergy, (1991) 67/5 (541-547).
ISSN: 0003-4738 CODEN: ANAEA3
COUNTRY: United States
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 011 Otorhinolaryngology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Second-generation H1 receptor antagonists (cetirizine, terfenadine, astemizole, loratadine, azelastine, and acrivastine) offer several important advantages over the older first-generation antihistamines. They are substantially less sedating and have little or no anticholinergic activity. Many of them are effective for 12 to 24 hours, thereby increasing compliance. In addition to acting as competitive inhibitors of histamine, several seem to have other antiallergic mechanisms as well. They are all absorbed well when taken orally. Many studies demonstrate their effectiveness compared with placebo in the treatment of seasonal and perennial rhinitis and chronic urticaria, and several studies suggest that they have a role in the treatment of bronchial asthma. A number of multicenter, double-blind, placebo-controlled studies comparing the effectiveness of terfenadine, 60 mg bid, with chlorpheniramine, 8 mg bid, in seasonal allergic rhinitis demonstrate that both drugs are approximately equally potent in reducing the symptoms of sneezing, rhinorrhea, and nasal itching and are statistically significantly better than placebo. Ocular symptoms were reduced somewhat less but still significantly. No differences from placebo were recorded in their effect on nasal congestion. The effectiveness of cetirizine, 10 mg once daily, compared with astemizole, 10 mg once daily, was measured in double-blind, placebo-controlled studies of patients with seasonal allergic rhinitis. These studies also demonstrate statistically significant benefit from the study drugs compared with placebo in relieving all nasal symptoms except congestion. Both drugs also relieved ocular pruritus. Fewer studies have assessed azelastine, acrivastine, and loratadine, but all have been shown

to provide significant relief of seasonal allergic rhinitis compared with placebo. There are a limited number of studies of second-generation H1 receptor antagonists in bronchial asthma. Studies of terfenadine, cetirizine, and azelastine versus placebo all demonstrate small but statistically significant improvement in bronchoconstriction and suggest that some relief of nocturnal asthma also may occur. Single-dose studies of the effect of cetrizine, terfenadine, and astemizole on wheal and flare demonstrate that cetirizine caused a significantly greater reduction than did either of the other two drugs at four to five hours. Other studies of chronic urticaria also reveal significant effectiveness of cetirizine and astemizole compared with placebo. All three drugs seem to be relatively equal in potency. In conclusion, the new second-generation H1 receptor antagonists are effective in treating the diseases for which antihistamines have traditionally been used and offer some hope of added benefit in the treatment of bronchial asthma. They seem to be similar in potency but offer the advantages of being relatively less sedating, nonanticholinergic, and having significantly longer durations of action.

L93 ANSWER 25 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 91068098 EMBASE
DOCUMENT NUMBER: 1991068098
TITLE: Second-generation H1-receptor antagonists.
AUTHOR: Estelle F.; Simons R.; Simons K.J.
CORPORATE SOURCE: Children's Hosp. of Winnipeg, 840 Sherbrook St.,Winnipeg, Man. R3A 1S1, Canada
SOURCE: Annals of Allergy, (1991) 66/1 (5-19).
ISSN: 0003-4738 CODEN: ANAEA3
COUNTRY: United States
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The second-generation H1-receptor antagonists do not penetrate into the central nervous system as readily as the first-generation H1-receptor antagonists do. They bind preferentially to peripheral rather than central H1-receptors. They cause no more sedation than placebo does. These medications differ considerably from one another in some aspects of basic pharmacology and in pharmacokinetics and pharmacodynamics. An understanding of these differences will facilitate their optimal clinical usage. The second-generation H1-receptor antagonists are replacing the first generation H1-receptor antagonists in the symptomatic treatment of allergic rhinoconjunctivitis, and in relieving pruritus in patients with urticaria. They have a mild beneficial effect in patients with chronic asthma. They have not supplanted the first generation H1-receptor antagonists in atopic dermatitis treatment or as adjunctive treatment of pruritus and other symptoms in patients with anaphylaxis.

L93 ANSWER 26 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90373187 EMBASE
DOCUMENT NUMBER: 1990373187
TITLE: Histamine and asthma.
AUTHOR: Wood-Baker R.; Church M.K.
CORPORATE SOURCE: Immunopharmacology Group, Clinical Pharmacology, Centre Block, Southampton General Hospital, Tremona Road, Southampton S09 4XY, United Kingdom
SOURCE: Immunology and Allergy Clinics of North America, (1990) 10/2 (329-336).
ISSN: 0889-8561 CODEN: INCAEP
COUNTRY: United States
DOCUMENT TYPE: Journal; **General Review**

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Histamine has been associated with the symptoms of allergic diseases for over 70 years. Its location in the secretory granule of mast cells lining the bronchial lumen would suggest that it is likely to be released following bronchial provocation of asthmatic subjects with inhaled allergen. This has now been demonstrated by observing changes in histamine levels in the circulation and in bronchoalveolar lavage fluid. Prophylaxis with histamine H1-receptor antagonists has shown that histamine contributes approximately 30% to the early-phase bronchoconstriction following allergen challenge but a higher contribution with adenosine or exercise provocation. In the treatment of clinical asthma, H1-antagonists afford a small bronchodilation and a marginal amelioration of disease. Further studies with the newer, more effective H1-antagonists are necessary to define more accurately their use in the treatment of asthma.

L93 ANSWER 27 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 89285439 EMBASE
DOCUMENT NUMBER: 1989285439
TITLE: Azelastine. A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential.
AUTHOR: McTavish D.; Sorkin E.M.
CORPORATE SOURCE: ADIS Drug Inform. Services, 41 Centorian Drive,Auckland 10, New Zealand
SOURCE: Drugs, (1989) 38/5 (778-800).
ISSN: 0012-6667 CODEN: DRUGAY
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Azelastine is an antiallergic agent which demonstrates histamine H1-receptor antagonist activity and also inhibits histamine release from mast cells following antigen and non-antigen stimuli. Azelastine antagonises histamine- and leukotriene-induced bronchospasm in animal studies and reduces airway responsiveness to inhaled antigen or distilled water, and exercise challenge. In comparative studies, orally administered azelastine in doses up to 4 mg/day consistently relieved symptoms in patients with seasonal or perennial rhinitis - comparable to inhaled sodium cromoglycate (cromolyn sodium) 80 mg/day, oral chlorpheniramine (chlorphenamine) and oral terfenadine 120 mg/day. In addition, azelastine administered as an intranasal spray was as effective as oral terfenadine 120 mg/day and intranasal budesonide 0.4 mg/day in alleviating symptoms of rhinitis. Azelastine is also a potent antiasthmatic agent which produces significant and long lasting bronchodilation in patients with bronchial asthma. The drug is superior to placebo and comparable to oral ketotifen 2 mg/day and sustained release theophylline 700 mg/day when administered as a twice daily oral 4 mg dose. Azelastine is generally well tolerated: the most common adverse effects are altered taste perception and drowsiness. Adverse effects are mild and transient and result in withdrawal of treatment in less than 2% of patients. In a comparative study oral azelastine 2 or 4 mg/day produced no more sedation than terfenadine 120 mg/day. Thus, barring unexpected findings with wider clinical use, azelastine offers an effective and well tolerated choice of treatment for patients with allergic rhinitis and/or bronchial asthma, which may be particularly beneficial in patients in whom inhaled drug treatment is

contraindicated.

```
=> fil medl; d que l30
FILE 'MEDLINE' ENTERED AT 13:02:48 ON 26 JUN 2003

 FILE LAST UPDATED: 25 JUN 2003 (20030625/UP). FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L3          2 SEA FILE=REGISTRY ABB=ON  LEVOCABASTINE?/CN
L7        212 SEA FILE=MEDLINE ABB=ON  LEVOCABASTIN# OR LIVOSTIN# OR
              LEVOPHTA OR R50547 OR R 50547 OR L3
L8     588794 SEA FILE=MEDLINE ABB=ON  C8./CT
L9     168638 SEA FILE=MEDLINE ABB=ON  HYPERSENSITIVITY+NT/CT
L10     13603 SEA FILE=MEDLINE ABB=ON  RHINITIS+NT/CT
L11      1313 SEA FILE=MEDLINE ABB=ON  CONJUNCTIVITIS, ALLERGIC/CT
L19     15312 SEA FILE=MEDLINE ABB=ON  PIPERIDINES/CT
L22     12267 SEA FILE=MEDLINE ABB=ON  L19(L)(AD OR PD OR PK OR TU)/CT
L23       108 SEA FILE=MEDLINE ABB=ON  L22/MAJ AND L7
L24    129176 SEA FILE=MEDLINE ABB=ON  (L8 OR L9 OR L10 OR L11)(L)(PC OR
              DT)/CT
L25     74032 SEA FILE=MEDLINE ABB=ON  L24/MAJ
L27    944399 SEA FILE=MEDLINE ABB=ON  GENERAL REVIEW/DT
L30        10 SEA FILE=MEDLINE ABB=ON  L23 AND L25 AND L27


=> s l30 not (l13 or l90)   previously printed

L94         9 L30 NOT (L13 OR L90)

=> fil embase; d que l77

FILE 'EMBASE' ENTERED AT 13:02:50 ON 26 JUN 2003
COPYRIGHT (C) 2003 Elsevier Science B.V. All rights reserved.

 FILE COVERS 1974 TO 19 Jun 2003 (20030619/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L33       568 SEA FILE=EMBASE ABB=ON  LEVOCABASTINE/CT
L35      1178 SEA FILE=EMBASE ABB=ON  ALLERGIC CONJUNCTIVITIS/CT
L36      1720 SEA FILE=EMBASE ABB=ON  ANTIALLERGIC AGENT/CT
L37    518140 SEA FILE=EMBASE ABB=ON  RESPIRATORY TRACT DISEASE+NT/CT
L38       607 SEA FILE=EMBASE ABB=ON  RHINOCONJUNCTIVITIS/CT
L39      7418 SEA FILE=EMBASE ABB=ON  ALLERGIC RHINITIS/CT
L40     23641 SEA FILE=EMBASE ABB=ON  ALLERGY/CT
L69    427343 SEA FILE=EMBASE ABB=ON  GENERAL REVIEW/DT
L73     92022 SEA FILE=EMBASE ABB=ON  (L35 OR (L37 OR L38 OR L39 OR L40))(L)(
              DT OR PC)/CT
L74     74199 SEA FILE=EMBASE ABB=ON  L73/MAJ OR L36/MAJ
L76       445 SEA FILE=EMBASE ABB=ON  L33(L)(DT OR PK OR DO OR AD OR PD)/CT
L77        13 SEA FILE=EMBASE ABB=ON  L76/MAJ AND L74 AND L69
```

```
=> s l77 not (145 or 187 or 191)

L95           9 L77 NOT (L45 OR L87 OR L91)

=> fil capl; d que 166                    previously printed

FILE 'CAPLUS' ENTERED AT 13:02:51 ON 26 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 26 Jun 2003  VOL 138 ISS 26
FILE LAST UPDATED: 25 Jun 2003  (20030625/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


L3            2 SEA FILE=REGISTRY ABB=ON  LEVOCABASTINE?/CN
L51         146 SEA FILE=CAPLUS ABB=ON  L3
L54        5895 SEA FILE=CAPLUS ABB=ON  RESPIRATORY TRACT/CW (L)(DISEASE# OR
               DISORDER#)
L55        2574 SEA FILE=CAPLUS ABB=ON  RHINITIS/OBI
L56          77 SEA FILE=CAPLUS ABB=ON  RHINOCONJUNCTIVITIS/OBI
L57       18906 SEA FILE=CAPLUS ABB=ON  ALLERGY/CT
L62         104 SEA FILE=CAPLUS ABB=ON  L51(L)(THU OR PAC OR BAC OR DMA OR
               PKT)/RL
L65     1643843 SEA FILE=CAPLUS ABB=ON  REVIEW/DT
L66           2 SEA FILE=CAPLUS ABB=ON  L62 AND (L54 OR L55 OR L56 OR L57) AND
               L65


=> s l66 not (153 or 188 or 192)

L96           1 L66 NOT (L53 OR L88 OR L92)

=> dup rem 194,196,195                    previously printed
FILE 'MEDLINE' ENTERED AT 13:03:13 ON 26 JUN 2003

FILE 'CAPLUS' ENTERED AT 13:03:13 ON 26 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 13:03:13 ON 26 JUN 2003
COPYRIGHT (C) 2003 Elsevier Science B.V.  All rights reserved.
PROCESSING COMPLETED FOR L94
PROCESSING COMPLETED FOR L96
PROCESSING COMPLETED FOR L95
```

L97 14 DUP REM L94 L96 L95 (5 DUPLICATES REMOVED)
ANSWERS '1-9' FROM FILE MEDLINE
ANSWERS '10-14' FROM FILE EMBASE

=> d ibib ab 1-14; fil hom

L97 ANSWER 1 OF 14 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 96191579 MEDLINE
DOCUMENT NUMBER: 96191579 PubMed ID: 8612470
TITLE: **Levocabastine**. An update of its pharmacology, clinical efficacy and tolerability in the topical treatment of allergic rhinitis and conjunctivitis.
AUTHOR: Noble S; McTavish D
CORPORATE SOURCE: Adis International Limited, Auckland, New Zealand.
SOURCE: DRUGS, (1995 Dec) 50 (6) 1032-49. Ref: 60
Journal code: 7600076. ISSN: 0012-6667.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960613
Last Updated on STN: 19960613
Entered Medline: 19960603

AB **Levocabastine** is a potent and selective histamine H1-receptor antagonist which has been evaluated as a topical treatment (nasal spray and/or eyedrops) for allergic rhinitis and/or conjunctivitis. Data available at the time of the previous review in Drugs, together with more recent results, have clearly demonstrated that **levocabastine** nasal spray and eyedrops are clinically effective, have a rapid onset of action and are well tolerated in patients with nasal and/or ocular allergic conditions. Previous evidence indicating that topical **levocabastine** has efficacy similar to or better than that of topical sodium cromoglycate (cromolyn sodium) has been confirmed in more recent studies. Furthermore, results from a number of controlled clinical trials have also shown that topical **levocabastine** is at least as effective as oral terfenadine for the treatment of allergic rhinoconjunctivitis. Notably, topical **levocabastine** appears to be more effective than oral terfenadine in improving the severity of selected symptoms. Limited data indicating efficacy equivalent to that of oral loratadine, oral cetirizine or azelastine nasal spray will need to be confirmed. Data from several studies have shown that topical **levocabastine** has a tolerability profile similar to that of placebo, topical sodium cromoglycate or oral terfenadine. The main adverse events seen in patients treated with topical **levocabastine** are ocular irritation after application of eyedrops, and headache, nasal irritation, somnolence and fatigue after administration of the nasal spray. Administered doses of topical **levocabastine**, and subsequent plasma concentrations, are low, and the risk of systemic adverse events is therefore expected to be minimal. Thus, topical administration of **levocabastine** rapid and effective symptom relief with no apparent serious adverse events in patients with allergic rhinitis and/or conjunctivitis. Topical **levocabastine** is a useful alternative to topical sodium cromoglycate or oral terfenadine. Additional data supporting current evidence that topical **levocabastine** can provide more effective symptom relief than oral terfenadine, together with clarification of the relative efficacies of these agents in relation to varying pollen exposure, would help to further confirm its clinical potential. However, the results available to date suggest that the topical formulations of **levocabastine** are a valuable treatment option in patients with allergic rhinitis and/or

conjunctivitis.

L97 ANSWER 2 OF 14 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 95308369 MEDLINE
DOCUMENT NUMBER: 95308369 PubMed ID: 7788568
TITLE: Topical **levocabastine**--an effective alternative to oral antihistamines in seasonal allergic rhinoconjunctivitis.
AUTHOR: Bahmer F A
CORPORATE SOURCE: Universitats-Hautklinik, Homburg/Saar, Germany.
SOURCE: CLINICAL AND EXPERIMENTAL ALLERGY, (1995 Mar) 25 (3) 220-7. Ref: 32
Journal code: 8906443. ISSN: 0954-7894.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199507
ENTRY DATE: Entered STN: 19950807
Last Updated on STN: 19950807
Entered Medline: 19950724

L97 ANSWER 3 OF 14 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 95037674 MEDLINE
DOCUMENT NUMBER: 95037674 PubMed ID: 7950341
TITLE: **Levocabastine** eye drops: a new approach for the treatment of acute allergic conjunctivitis.
AUTHOR: Abelson M B; Weintraub D
CORPORATE SOURCE: Schepens Eye Research Institute, Boston, Massachusetts.
SOURCE: EUROPEAN JOURNAL OF OPHTHALMOLOGY, (1994 Apr-Jun) 4 (2) 91-101. Ref: 40
Journal code: 9110772. ISSN: 1120-6721.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941208

AB Acute allergic conjunctivitis (AAC) is a common ocular allergic disorder and incident rates as high as 20% have been reported. Although a wide range of therapeutic agents are available for the treatment of AAC, the ideal treatment seems to have remained elusive. **Levocabastine**, a highly potent specific H1-receptor, appears to offer a promising alternative as a topical single-agent therapy. **Levocabastine** eye drops have been found to be well tolerated with an adverse-effect profile comparable to placebo and sodium cromoglycate. In addition, ocular **levocabastine** has been shown to have a rapid onset and long duration of action. The efficacy of **levocabastine** has been extensively investigated in conjunctival provocation tests and environmental studies. The available data suggest that ocular **levocabastine** is an effective therapeutic agent. Statistically significant differences in favour of **levocabastine** have been observed in comparisons with sodium cromoglycate, antazoline/naphazoline and oral terfenadine.

L97 ANSWER 4 OF 14 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 91243596 MEDLINE

DOCUMENT NUMBER: 91243596 PubMed ID: 1709851
TITLE: **Levocabastine**. A review of its pharmacological properties and therapeutic potential as a topical antihistamine in allergic rhinitis and conjunctivitis.
AUTHOR: Dechant K L; Goa K L
CORPORATE SOURCE: Adis Drug Information Services, Auckland, New Zealand.
SOURCE: DRUGS, (1991 Feb) 41 (2) 202-24. Ref: 26
Journal code: 7600076. ISSN: 0012-6667.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199107
ENTRY DATE: Entered STN: 19910719
Last Updated on STN: 19960129
Entered Medline: 19910702

AB **Levocabastine** is a long acting, highly potent and selective histamine H1-receptor antagonist, which has been developed for nasal and ocular administration. In controlled trials performed to date **levocabastine** was effective and well tolerated in the treatment of allergic rhinitis and allergic conjunctivitis. Comparative studies have demonstrated that **levocabastine** is superior to placebo and at least as effective as sodium cromoglycate (cromolyn sodium) in alleviating symptoms associated with seasonal allergic conditions. Although **levocabastine** appears to be less effective than the topical corticosteroid beclomethasone with regard to relieving runny and blocked nose, further comparative trials between these 2 agents would be desirable. Similar to other antihistamines, **levocabastine** provides minimal relief of nasal blockage, but this symptom is believed to be mediated by receptors other than histamine H1. The prompt onset of antiallergic activity after application differentiates **levocabastine** from the reference topical antiallergic, sodium cromoglycate, which has an onset of efficacy characterised by a lag period, thereby necessitating maintenance treatment. The incidence of adverse effects associated with **levocabastine** therapy is low and is similar to that observed with placebo and sodium cromoglycate. **Levocabastine** provides prophylactic protection as well as acute relief from nasal and ocular symptoms in patients with seasonal allergic disorders. With the ever increasing trend towards topical therapy for the treatment of allergic rhinitis and allergic conjunctivitis, **levocabastine** is a useful addition to the range of drugs currently available. Possible avenues for additional research should include determining whether the antiallergic efficacy of topical **levocabastine** is superior to that of oral agents such as astemizole and terfenadine, and whether topical therapy is indeed preferred, considering the relative ease of administration of effective oral antiallergic agents.

L97 ANSWER 5 OF 14 MEDLINE
ACCESSION NUMBER: 94304752 MEDLINE
DOCUMENT NUMBER: 94304752 PubMed ID: 7913336
TITLE: The role of **levocabastine** in the treatment of allergic rhinoconjunctivitis.
AUTHOR: Knight A
CORPORATE SOURCE: Division of Clinical Immunology, Sunnybrook Hospital University of Toronto Clinic, Ontario, Canada.
SOURCE: BRITISH JOURNAL OF CLINICAL PRACTICE, (1994 May-Jun) 48 (3) 139-43. Ref: 44
Journal code: 0372546. ISSN: 0007-0947.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 19940825
Last Updated on STN: 19950206
Entered Medline: 19940818

AB Allergic rhinoconjunctivitis is a common atopic condition frequently encountered in clinical practice, with prevalence figures as high as 20% reported. The socioeconomic impact of this condition is considerable--not only in terms of medical costs but lost work and schooldays and quality of life. A wide range of therapeutic approaches is available, including **levocabastine**, an extremely potent and highly specific H1-receptor antagonist which has been developed for topical application as eyedrops and nasal spray. The available clinical data demonstrate that this agent is well tolerated, with an adverse effect profile comparable to sodium cromoglycate and placebo. Onset of action is rapid, with maximum therapeutic effects typically being observed within minutes of application. Results of comparative clinical trials suggest that topical **levocabastine** is as at least as effective as oral antihistamines and sodium cromoglycate for the treatment of allergic rhinoconjunctivitis, and it is suggested as an attractive alternative to oral antihistamines as first-line therapeutic option.

L97 ANSWER 6 OF 14 MEDLINE
ACCESSION NUMBER: 93314560 MEDLINE
DOCUMENT NUMBER: 93314560 PubMed ID: 1363981
TITLE: New trends in the treatment of allergic conjunctivitis.
AUTHOR: Parys W; Blockhuys S; Janssens M
CORPORATE SOURCE: Janssen Research Foundation, Beerse, Belgium.
SOURCE: DOCUMENTA OPHTHALMOLOGICA, (1992) 82 (4) 353-60. Ref: 15
Journal code: 0370667. ISSN: 0012-4486.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930820
Last Updated on STN: 19950206
Entered Medline: 19930809

AB Histamine is the key mediator producing itching, redness and chemosis in allergic conjunctivitis. Histamine levels in tears are increased ten-fold in patients with this allergic condition. **Levocabastine** is a newly synthesized histamine H1 antagonist which has been formulated as both eye drops and nasal spray. In well established assays of antihistamine activity, **levocabastine** was found to be the most potent antihistamine compound available, being 15,000 times more potent than chlorpheniramine. Ocular provocation studies in man have shown that **levocabastine** protects against the symptoms of allergen-induced conjunctivitis. Ophthalmological examinations, including slit lamp and ophthalmoscopy showed no adverse effects. Data from therapeutic studies are available for more than 1700 patients with allergic conjunctivitis treated for 2-16 weeks. One drop of **levocabastine** (0.5 mg/ml) per eye given two to four times daily provided significantly better symptom control than placebo, with good to excellent results in 71% of patients on **levocabastine** compared to 55% on placebo ($p < 0.001$). **Levocabastine** has a fast onset of action. In one study 94% of patients experienced symptom relief within 15 minutes after the first instillation. The effects observed with **levocabastine**

were at least as good as those with ocular cromoglycate or oral terfenadine. The incidence of adverse experiences was not different from placebo. **Levocabastine** promises to be a valuable treatment for patients with allergic conjunctivitis.

L97 ANSWER 7 OF 14 MEDLINE
ACCESSION NUMBER: 93314559 MEDLINE
DOCUMENT NUMBER: 93314559 PubMed ID: 1363980
TITLE: Efficacy of **levocabastine** in conjunctival provocation studies.
AUTHOR: Janssens M
CORPORATE SOURCE: Janssen Research Foundation, Beerse, Belgium.
SOURCE: DOCUMENTA OPHTHALMOLOGICA, (1992) 82 (4) 341-51. Ref: 16
Journal code: 0370667. ISSN: 0012-4486.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930820
Last Updated on STN: 19950206
Entered Medline: 19930809

AB **Levocabastine** is a new topical histamine H1 antagonist. The antihistaminic and antiallergic effects of **levocabastine** eye drops have been evaluated in eight conjuctival provocation studies (n = 238). Two studies used a histamine challenge; five studies used allergen challenge; one study used both and in one study allergic provocation was with compound 48/80. In all but one study, only one single dose of **levocabastine** (one or two drops) was given. Six studies were against placebo only; one was against cromoglycate and one study used both placebo and cromoglycate as reference drugs. Single instillation of **levocabastine** eye drops protected against histamine and allergen-induced ocular symptoms within a period of 10 minutes. **Levocabastine** eye drops significantly alleviated conjunctival itching, redness, chemosis, eyelid swelling and tearing induced by histamine or allergen challenge ($p < or = 0.05$). Four hours after administration **levocabastine** was still active. With **levocabastine**, but not with cromoglycate, a significant increase was observed in the allergen threshold. Even when compared to cromoglycate given as a pre-treatment four times daily for two weeks before the allergen challenge, a single dose of **levocabastine** was significantly more effective in inhibiting hyperaemia, eyelid swelling, chemosis and tearing (all $p < 0.05$). In conclusion, conjunctival provocation studies have established that **levocabastine** has a rapid and long-lasting effect in protecting against histamine or allergen-induced conjunctival symptoms.

L97 ANSWER 8 OF 14 MEDLINE
ACCESSION NUMBER: 93040514 MEDLINE
DOCUMENT NUMBER: 93040514 PubMed ID: 1358140
TITLE: **Levocabastine**: a new topical approach for the treatment of paediatric allergic rhinoconjunctivitis.
AUTHOR: Janssens M M
CORPORATE SOURCE: Dept. of Clinical Research and Development, Janssen Research Foundation, Beerse, Belgium.
SOURCE: RHINOLOGY. SUPPLEMENT, (1992 Sep) 13 39-49. Ref: 13
Journal code: 9004674. ISSN: 1013-0047.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, MULTICASE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19950206
Entered Medline: 19921203

AB **Levocabastine** is a novel H1-receptor antagonist for topical use, which is being investigated in allergic rhinitis (nasal spray) and conjunctivitis (eye drops). Its anti-allergic effects have been demonstrated in nasal and ocular provocation tests. Clinical studies have been performed in 1,363 patients with allergic rhinitis and 1,218 patients with allergic conjunctivitis, comparing **levocabastine** mainly to placebo and cromoglycate. **Levocabastine** was effective when used at a dose of 2 sprays per nostril or 1 drop per eye twice daily, which if necessary can be increased up to four times daily. **Levocabastine** was superior to placebo in alleviating symptoms such as sneezing, itchy nose, runny nose, itchy eyes, red eyes and lacrimation. In global evaluations some 60% of patients had good to excellent results with the nasal spray and some 75% with the eye drops. **Levocabastine** was shown to be as good or even slightly better than cromoglycate. Onset of action was fast, with 73% of patients reporting symptom relief within 30 min after administration of **levocabastine** nasal spray. Adverse experiences were similar in type and incidence with **levocabastine** , cromoglycate and placebo, for nasal spray as well as eye drops. The most frequent complaints were nasal and ocular irritation, respectively, with a similar incidence for the three drugs. Limited data are available in children so far, but they indicate response rate and adverse-experience profile to be similar to what was observed in adults. **Levocabastine**, thus, is an interesting new antihistamine available for topical use in allergic rhinoconjunctivitis. It has been extensively evaluated in adults, and preliminary data indicate that it can also be useful in allergic children.

L97 ANSWER 9 OF 14 MEDLINE
ACCESSION NUMBER: 92004910 MEDLINE
DOCUMENT NUMBER: 92004910 PubMed ID: 1680536
TITLE: **Levocabastine**: an effective topical treatment of allergic rhinoconjunctivitis.
AUTHOR: Janssens M M; Vanden Bussche G
CORPORATE SOURCE: Department of Clinical Research and Development, Janssen Research Foundation, Beerse, Belgium.
SOURCE: CLINICAL AND EXPERIMENTAL ALLERGY, (1991 May) 21 Suppl 2 29-36. Ref: 67
Journal code: 8906443. ISSN: 0954-7894.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199111
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19950206
Entered Medline: 19911106

AB The new H1-receptor antagonist **levocabastine** is the most potent antihistamine available, as shown in classical animal tests for antihistamine activity. Its effects also are very specific, with doses as high as 40,000 times the effective antihistamine dose not displaying other pharmacological effects. In nasal and ocular provocation tests, **levocabastine** nasal spray and eye drops protected against allergen-induced nasal and ocular symptoms. Twenty-three clinical trials have been performed with **levocabastine** nasal spray in 1363 patients with allergic rhinitis. At a dose of two sprays per nostril

twice daily (if necessary to be increased up to four times daily), **levocabastine** was significantly better than placebo and as good as or slightly better than cromoglycate in alleviating nasal symptoms. Good to excellent results were reported in about 60% of patients on **levocabastine**, compared with 37% with placebo and 47% with cromoglycate. **Levocabastine** eye drops were studied in 21 clinical trials including 1218 patients with allergic conjunctivitis. One drop per eye twice daily (up to four times daily) provided significantly better symptom control than placebo and similar effects as those observed with cromoglycate. Response rates were 71-80% with **levocabastine**, 55% with placebo and 76% with cromoglycate. **Levocabastine** has a fast onset of action, with 94% of patients experiencing symptom relief within 15 min after the first instillation of **levocabastine** eye drops. Three long-term studies (10-16 weeks' duration) showed absence of tachyphylaxis during prolonged treatment with **levocabastine**. The incidence of adverse experiences was similar for **levocabastine**, cromoglycate and placebo, for nasal spray as well as eye drops.(ABSTRACT TRUNCATED AT 250 WORDS)

L97 ANSWER 10 OF 14 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002135212 EMBASE
TITLE: Pharmacological and clinical properties of levocabastine hydrochloride (eye drop and nasal spray), a selective H(1) antagonist.
AUTHOR: Akiyoshi M.; Shigeoka T.; Torii S.; Maki E.; Enomoto S.; Takahashi H.; Hirano F.
CORPORATE SOURCE: M. Akiyoshi, Nonclinical Group, Janssen Pharmaceutical K.K., 1-5 Higashi-gotanda, Shinagawa-ku, Tokyo 141-8633, Japan. makiyosh@janjp.jnj.com
SOURCE: Folia Pharmacologica Japonica, (2002) 119/3 (175-184).. Refs: 31
ISSN: 0015-5691 CODEN: NYKZAU
COUNTRY: Japan
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
AB Levocabastine is a selective histamine H(1)-receptor antagonist exerting inhibitory effects on the release of chemical mediators from mast cells and on the chemotaxis of polymorphonuclear leukocytes and eosinophils. Both histamine and antigens induced conjunctivitis was inhibited by levocabastine in several allergy models. Levocabastine moderately inhibited histamine-release from guinea pig conjunctive induced by antigen-antibody reactions and prevented an increase in the vascular permeability of the conjunctive elicited by both histamine and antigen instillation. Symptoms of allergic rhinitis, which were induced by histamine, substance P and antigen, were also reduced by levocabastine. Levocabastine prevented an increase in the vascular permeability of nasal mucosa elicited by instillation of these three inducers. Furthermore, levocabastine has shown a large difference between the antiallergic dose and other non-specific pharmacological effective dose than that with other antiallergic drugs. The non-specific pharmacological effect of levocabastine reveals only blepharoptosis. With these pharmacological effects and topical usage, levocabastine was shown to be useful for allergic conjunctive and rhinitis in both seasonal and perennial clinical use.

L97 ANSWER 11 OF 14 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95310141 EMBASE
DOCUMENT NUMBER: 1995310141
TITLE: The pharmacokinetic properties of topical levocabastine. A

review.
AUTHOR: Heykants J.; Van Peer A.; Van de Velde V.; Snoeck E.; Meuldermans W.; Woestenborghs R.
CORPORATE SOURCE: Dept Drug Metabol Pharmacokinetics, Janssen Research Foundation,B-2340 Beerse, Belgium
SOURCE: Clinical Pharmacokinetics, (1995) 29/4 (221-230). ISSN: 0312-5963 CODEN: CPKNDH
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 011 Otorhinolaryngology
012 Ophthalmology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The linear and predictable pharmacokinetic properties of the histamine H1-receptor antagonist levocabastine make it particularly suitable for intranasal or ocular treatment of allergic rhinoconjunctivitis. Peak plasma concentrations (C(max)) occur within 1 to 2 hours of administration of single doses of levocabastine nasal spray and eye drops (0.2 mg and 0.04 mg, respectively). Drug absorption is incomplete after intranasal and ocular administration, with systemic availability ranging from 60 to 80% for levocabastine nasal spray and from 30 to 60% for the eye drops. However, as the amount of levocabastine applied intranasally and ocularly is small, the levocabastine plasma concentrations achieved are extremely low, with C(max) values in the ranges 1.4 to 2.2 .mu.g/L and 0.26 to 0.29 .mu.g/L for intranasal and ocular administration, respectively. Pharmacokinetic-pharmacodynamic modelling has indicated that the clinical benefits of levocabastine are predominantly mediated through local antihistaminic effects, although some systemic activity may contribute to the therapeutic efficacy of levocabastine nasal spray during long term use. Levocabastine undergoes minimal hepatic metabolism, i.e. ester glucuronidation, and is predominantly cleared by the kidneys. Approximately 70% of parent drug is recovered unchanged in the urine. Plasma protein binding is approximately 55% and the potential for drug interactions involving binding site displacement is negligible, Furthermore, the pharmacokinetics of this agent do notappear to be influenced by either age or gender. Levocabastine nasal spray and eye drops may thus be considered suitable for the treatment of allergic rhinoconjunctivitis in a wide patient population.

L97 ANSWER 12 OF 14 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95203253 EMBASE
DOCUMENT NUMBER: 1995203253
TITLE: Treatment of allergic rhinoconjunctivitis: A review of the role of topical levocabastine.
AUTHOR: Van Wijk R.G.
CORPORATE SOURCE: Academisch Ziekenhuis Dijkzigt,Rotterdam, Netherlands
SOURCE: Mediators of Inflammation, (1995) 4/SUPPL. 1 (S31-S38). ISSN: 0962-9351 CODEN: MNFLEF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 012 Ophthalmology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Levocabastine is an extremely potent and highly selective H1-receptor antagonist which has been specifically developed as eye drops and nasal spray for the treatment of allergic rhinoconjunctivitis. Clinical experience to date suggests that this topical antihistamine is at least as effective as other current first-line therapeutic approaches for the

treatment of this condition, including oral H1-receptor antagonists and sodium cromoglycate. Onset of action is rapid, with clinical effects apparent within minutes of instillation. Moreover, duration of action is sufficiently long to permit a convenient twice-daily dosing regimen. Topical levocabastine is well tolerated with an adverse-effect profile comparable with that of placebo and sodium cromoglycate. As might be expected from the route of drug administration, application site reactions are the most frequent adverse effect associated with levocabastine eye drops and nasal spray with an incidence comparable with that seen in placebo-treated controls. The availability of effective and well-tolerated topical antihistamines, such as levocabastine, is an important advance which broadens the range of therapeutic approaches available for the clinical management of allergic rhinoconjunctivitis. Levocabastine appears to be an attractive alternative to oral antihistamines as a first-line therapeutic option for the treatment of this atopic condition.

L97 ANSWER 13 OF 14 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95246175 EMBASE
DOCUMENT NUMBER: 1995246175
TITLE: Allergic and atopic diseases of the lid, conjunctiva, and cornea.
AUTHOR: Spraul C.W.; Lang G.K.
CORPORATE SOURCE: Poliklinik in Ulm, Universitats-Augenklinik, Prittwitzstrasse 43,D-89075 Ulm, Germany
SOURCE: Current Opinion in Ophthalmology, (1995) 6/4 (21-26). ISSN: 1040-8738 CODEN: COOTEF
COUNTRY: United States
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Ocular allergies are commonly encountered in clinical practice. The familiarity with the typical constellation of signs and symptoms, as well as the pathophysiology of these syndromes, is of utmost importance in diagnosing and treating these diseases. Several new therapeutic options have been tested in clinical settings in recent time. Lodoxamine tromethamine is a mast cell stabilizer at least as effective as cromolyn sodium, which is currently not available in the United States. Nedocromil sodium in addition to its mast cell stabilizing effect, has anti-inflammatory properties. Levocabastine hydrochloride is a very selective and potent H1 antihistamine. Ketorolac tromethamine is a topical nonsteroidal anti-inflammatory agent.

L97 ANSWER 14 OF 14 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90029432 EMBASE
DOCUMENT NUMBER: 1990029432
TITLE: Management of allergic rhinitis: Focus on intranasal agents.
AUTHOR: Dushay M.E.; Johnson C.E.
CORPORATE SOURCE: Department of Pharmacy Services, William Beaumont Hospital, Royal Oak, MI, United States
SOURCE: Pharmacotherapy, (1989) 9/6 (338-350). ISSN: 0277-0008 CODEN: PHPYDQ
COUNTRY: United States
DOCUMENT TYPE: Journal; **General Review**
FILE SEGMENT: 011 Otorhinolaryngology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The clinical manifestations of allergic rhinitis are the result of an immune-mediated process after exposure of a sensitized individual to

airborne allergens. The primary symptomatology includes nasal congestion, rhinorrhea, nasal and conjunctival pruritus, and sneezing. Principles of management include allergen avoidance, palliative therapy, immunotherapy, and pharmacotherapy. Oral decongestants stimulate .alpha.-adrenergic receptors in the nasal cavity, resulting in vasoconstriction and decreased edema. Oral antihistamines block histaminel (H1) receptors, and may relieve rhinorrhea, sneezing, and nasal and conjunctival pruritus. Topical decongestants have a local effect on adrenergic receptors in the nasal mucosa, resulting in rapid, marked vasoconstriction. Intranasal corticosteroids inhibit mediator release from mast cells and basophils, and reduce edema of the nasal mucosa. Dexamethasone sodium phosphate, beclomethasone dipropionate, and flunisolide are currently available for intranasal administration. Cromolyn sodium inhibits allergen-induced degranulation and mediator release from sensitized cells, and is useful primarily as a prophylactic agent. Several agents, including the corticosteroids budesonide and flucortin butylester, the mast cell-stabilizing agent nedocromil sodium, the anticholololinergic agent ipratropium bromide, and the H1 receptor antagonist levocabastine are being investigated for intranasal use in the management of allergic rhinitis.

FILE 'HOME' ENTERED AT 13:03:24 ON 26 JUN 2003